



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C12N 15/12	A1	(11) International Publication Number: WO 00/58463 (43) International Publication Date: 5 October 2000 (05.10.00)
<p>(21) International Application Number: PCT/NZ00/00015</p> <p>(22) International Filing Date: 18 February 2000 (18.02.00)</p> <p>(30) Priority Data: 09/276,268 25 March 1999 (25.03.99) US 09/383,586 26 August 1999 (26.08.99) US</p> <p>(71) Applicant (for all designated States except US): GENESIS RESEARCH & DEVELOPMENT CORPORATION LIMITED [NZ/NZ]; 1 Fox Street, Parnell, Auckland (NZ).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): STRACHAN, Lorna [GB/NZ]; 11/50 Livingstone Street, Coss Bay, Auckland (NZ). SLEEMAN, Matthew [GB/NZ]; 19 Derwent Crescent, Titirangi, Auckland (NZ). ABERNETHY, Nevin [CA/NZ]; 2 Worcester Road, Meadowbank, Auckland (NZ). ONRUST, Rene [NZ/NZ]; 21 Duart Avenue, Mt. Albert, Auckland (NZ). KUMBLE, Krishanand, D. [IN/NZ]; 2301 S Millbend Drive #706, The Woodlands, TX 77380 (US). MURISON, James, Greg [NZ/NZ]; 24 Calgary Street, Sandringham, Auckland (NZ).</p>	<p>(74) Agents: BENNETT, Michael, Roy et al.; West-Walker Bennett, Mobil on the Park, 157 Lambton Quay, Wellington (NZ).</p> <p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report.</p>	
<p>(54) Title: POLYNUCLEOTIDE AND DEDUCED AMINO ACID SEQUENCES FROM STROMAL CELLS</p> <p>(57) Abstract</p> <p>Isolated polynucleotides encoding polypeptides expressed in mammalian <i>fsn</i> -- lymph node stromal cells are provided, together with expression vectors and host cells comprising such isolated polynucleotides. Methods for the use of such polynucleotides and polypeptides are also provided.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

5

Polynucleotide and deduced amino acid sequences from stromal cells

10 Technical Field of the Invention

This invention relates to genes encoding proteins expressed in lymph node stromal cells from flaky skin (*fsn -/-*) mice and their use in therapeutic methods.

Background of the Invention

15 Lymph vessels and nodes are important components of the body's immune system. Lymph nodes are small lymphatic organs that are located in the path of lymph vessels. Large molecules and cells, including foreign substances, enter into the lymphatic vessels and, in circulating through these vessels, pass through the lymph nodes. Here, any foreign substances are concentrated and exposed to lymphocytes. This triggers a cascade of events that constitute
20 an immune response, protecting the body from infection and from cancer.

Lymph nodes are surrounded by a dense connective tissue network that forms a supporting capsule. This network extends into the body of the lymph node, forming an additional framework of support. Throughout the remainder of the organ, a fine meshwork can be identified that comprises reticular fibres and the reticular cells that produce and surround the
25 fibres. These features provide a support for the main functional cells of the lymphatic system, which are T- and B-lymphocytes. Additional cell types found in lymph nodes include macrophages, follicular dendritic cells, and endothelial cells that line the blood vessels servicing the node.

The cells within lymph nodes communicate with each other in order to defend the body
30 against foreign substances. When a foreign substance, or antigen, is present, it is detected by macrophages and follicular dendritic cells that take up and process the antigen, and display parts of it on their cell surface. These cell surface antigens are then presented to T- and B-lymphocytes, causing them to proliferate and differentiate into activated T-lymphocytes and plasma cells, respectively. These cells are released into the circulation in order to seek out and
35 destroy antigen. Some T- and B-lymphocytes will also differentiate into memory cells. Should these cells come across the same antigen at a later date, the immune response will be more rapid.

5 Once activated T- and B-lymphocytes are released into the circulation, they can perform a variety of functions that leads to the eventual destruction of antigen. Activated T-lymphocytes can differentiate into cytotoxic lymphocytes (also known as killer T-cells) which recognise other cells that have foreign antigens on their surface and kill the cell by causing them to lyse. Activated T-lymphocytes can also differentiate into helper T-cells which will then secrete
10 proteins in order to stimulate B-lymphocytes, and other T-lymphocytes, to respond to antigens. In addition, activated T-lymphocytes can differentiate into suppressor T-cells which secrete factors that suppress the activity of B-lymphocytes. Activated B-lymphocytes differentiate into plasma cells, which synthesise and secrete antibodies that bind to foreign antigens. The antibody-antigen complex is then detected and destroyed by macrophages, or by a group of
15 blood constituents known as complement.

 Lymph nodes can be dissociated and the resulting cells grown in culture. Cells that adhere to the tissue culture dishes can be maintained for some length of time and are known as stromal cells. The cultured cells are a heterogeneous population and can be made up of most cells residing within lymph nodes, such as reticular cells, follicular dendritic cells, macrophages
20 and endothelial cells. It is well known that bone marrow stromal cells play a critical role in homing, growth and differentiation of hematopoietic progenitor cells. Proteins produced by stromal cells are necessary for the maintenance of plasma cells *in vitro*. Furthermore, stromal cells are known to secrete factors and present membrane-bound receptors that are necessary for the survival of lymphoma cells.

25 An autosomal recessive mutation, designated flaky skin (*fsn* -/-), has been described in the inbred A/J mouse strain (The Jackson Laboratory, Bar Harbour, ME). The mice have a skin disorder similar to psoriasis in humans. Psoriasis is a common disease affecting 2% of the population, which is characterised by a chronic inflammation associated with thickening and scaling of the skin. Histology of skin lesions shows increased proliferation of the cells in the
30 epidermis, the uppermost layer of skin, together with the abnormal presence of inflammatory cells, including lymphocytes, in the dermis, the layer of skin below the epidermis. While the cause of the disease is unclear, psoriasis is associated with a disturbance of the immune system involving T lymphocytes. The disease occurs more frequently in family members, indicating the involvement of a genetic factor as well. Mice with the *fsn* gene mutation have not only a
35 psoriatic-like skin disease but also other abnormalities involving cells of the immune and

5 hematopoietic system. These mice have markedly increased numbers of lymphocytes associated with enlarged lymphoid organs, including the spleen and lymph nodes. In addition, their livers are enlarged, and the mice are anaemic. Genes and proteins expressed in abnormal lymph nodes of *fsn*^{-/-} mice may thus influence the development or function of cells of the immune and hematopoietic system, the response of these cells in inflammatory disorders, and the responses of
10 skin and other connective tissue cells to inflammatory signals.

There is a need in the art to identify genes encoding proteins that function to modulate all cells of the immune system. These proteins from normal or abnormal lymph nodes may be useful in modifying the immune responses to tumour cells or infectious agents such as bacteria, viruses, protozoa and worms. Such proteins may be useful in the treatment of disorders where
15 the immune system initiates unfavourable reactions to the body, including Type I hypersensitivity reactions (such as hay fever, eczema, allergic rhinitis and asthma), and Type II hypersensitivity reactions (such as transfusion reactions and haemolytic disease of newborns). Other unfavourable reactions are initiated during Type III reactions, which are due to immune complexes forming in infected organs during persistent infection or in the lungs following
20 repeated inhalation of materials from moulds, plants or animals, and in Type IV reactions in diseases such as leprosy, schistosomiasis and dermatitis.

Novel proteins of the immune system may also be useful in treating autoimmune diseases where the body recognises itself as foreign. Examples of such diseases include rheumatoid arthritis, Addison's disease, ulcerative colitis, dermatomyositis and lupus. Such proteins may
25 also be useful during tissue transplantation, where the body will often recognise the transplanted tissue as foreign and attempt to kill it, and also in bone marrow transplantation when there is a high risk of graft-versus-host disease where the transplanted cells attack their host cells, often causing death.

There thus remains a need in the art for the identification and isolation of genes encoding
30 proteins expressed in cells of the immune system for use in the development of therapeutic agents for the treatment of disorders including those associated with the immune system.

5 Summary of the Invention

 The present invention provides polypeptides expressed in lymph node stromal cells of *fsn* -/- mice, together with polynucleotides encoding such polypeptides, expression vectors and host cells comprising such polynucleotides, and methods for their use.

 In specific embodiments, isolated polypeptides are provided that comprise an amino acid
10 sequence selected from the group consisting of sequences provided in SEQ ID NO: 11-20, 30-38
 and 47-53, and variants of such sequences, as defined herein. Isolated polypeptides which
 comprise at least a functional portion of a polypeptide comprising an amino acid sequence
 selected from the group consisting of: (a) sequences provided in SEQ ID NO: 11-20, 30-38 and
 47-53; and (b) variants of a sequence of SEQ ID NO: 11-20, 30-38 and 47-53, as defined herein,
15 are also provided.

 In other embodiments, the present invention provides isolated polynucleotides
 comprising a nucleotide sequence selected from the group consisting of: (a) sequences provided
 in SEQ ID NO: 1-10, 21-29 and 39-46; (b) complements of sequences provided in SEQ ID NO:
 1-10, 21-29 and 39-46; (c) reverse complements of sequences provided in SEQ ID NO: 1-10, 21-
20 29 and 39-46; (d) reverse sequences of sequences provided in SEQ ID NO: 1-10, 21-29 and 39-
 46; and (e) variants of the sequences of (a) – (d), as defined herein.

 In related embodiments, the present invention provides expression vectors comprising the
 above polynucleotides, together with host cells transformed with such vectors.

 As detailed below, the isolated polynucleotides and polypeptides of the present invention
25 may be usefully employed in the preparation of therapeutic agents for the treatment of
 immunological disorders.

 In related embodiments, methods for modulating the growth of blood vessels, and for the
 treatment of disorders such as inflammatory disorders, disorders of the immune system, cancer,
 tumour-necrosis factor-mediated disorders, and viral disorders are provided. Examples of such
30 disorders include HIV-infection; epithelial, lymphoid, myeloid, stromal and neuronal cancers;
 arthritis; inflammatory bowel disease; and cardiac failure.

 The above-mentioned and additional features of the present invention, together with the
 manner of obtaining them, will be best understood by reference to the following more detailed
 description. All references disclosed herein are hereby incorporated by reference in their entirety
35 as if each was incorporated individually.

5

Detailed Description of the Invention

In one aspect, the present invention provides polynucleotides isolated from lymph node stromal cells of *fsn* ^{-/-} mice and isolated polypeptides encoded by such polynucleotides.

The term "polynucleotide(s)," as used herein, means a single or double-stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and corresponding RNA molecules, including HnRNA and mRNA molecules, both sense and anti-sense strands, and comprehends cDNA, genomic DNA and recombinant DNA, as well as wholly or partially synthesized polynucleotides. An HnRNA molecule contains introns and corresponds to a DNA molecule in a generally one-to-one manner. An mRNA molecule corresponds to an HnRNA and DNA molecule from which the introns have been excised. A polynucleotide may consist of an entire gene, or any portion thereof. Operable anti-sense polynucleotides may comprise a fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes all such operable anti-sense fragments. Anti-sense polynucleotides and techniques involving anti-sense polynucleotides are well known in the art and are described, for example, in Robinson-Benion *et al.*, *Methods in Enzymol.* 254: 363-375, 1995 and Kawasaki *et al.*, *Artific. Organs* 20: 836-848, 1996.

In specific embodiments, the isolated polynucleotides of the present invention comprise a DNA sequence selected from the group consisting of sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46.

Complements of such isolated polynucleotides, reverse complements of such isolated polynucleotides and reverse sequences of such isolated polynucleotides are also provided, together with polynucleotides comprising at least a specified number of contiguous residues (x-mers) of any of the above-mentioned polynucleotides, extended sequences corresponding to any of the above polynucleotides, antisense sequences corresponding to any of the above polynucleotides, and variants of any of the above polynucleotides, as that term is described in this specification.

The definition of the terms "complement", "reverse complement" and "reverse sequence", as used herein, is best illustrated by the following example. For the sequence 5' AGGACC 3', the complement, reverse complement and reverse sequence are as follows:

5	complement	3' TCCTGG 5'
	reverse complement	3' GGTCCT 5'
	reverse sequence	5' CCAGGA 3'.

Some of the polynucleotides of the present invention are "partial" sequences, in that they do not represent a full length gene encoding a full length polypeptide. Such partial sequences may be extended by analyzing and sequencing various DNA libraries using primers and/or probes and well known hybridization and/or PCR techniques. Partial sequences may be extended until an open reading frame encoding a polypeptide, a full length polynucleotide and/or gene capable of expressing a polypeptide, or another useful portion of the genome is identified. Such extended sequences, including full length polynucleotides and genes, are described as "corresponding to" a sequence identified as one of the sequences of SEQ ID NO: 1-10, 21-29 and 39-46, or a variant thereof, or a portion of one of the sequences of SEQ ID NO: 1-10, 21-29 and 39-46, or a variant thereof, when the extended polynucleotide comprises an identified sequence or its variant, or an identified contiguous portion (x-mer) of one of the sequences of SEQ ID NO: 1-10, 21-29 and 39-46, or a variant thereof. Such extended polynucleotides may have a length of from about 50 to about 4,000 nucleic acids or base pairs, and preferably have a length of less than about 4,000 nucleic acids or base pairs, more preferably yet a length of less than about 3,000 nucleic acids or base pairs, more preferably yet a length of less than about 2,000 nucleic acids or base pairs. Under some circumstances, extended polynucleotides of the present invention may have a length of less than about 1,800 nucleic acids or base pairs, preferably less than about 1,600 nucleic acids or base pairs, more preferably less than about 1,400 nucleic acids or base pairs, more preferably yet less than about 1,200 nucleic acids or base pairs, and most preferably less than about 1,000 nucleic acids or base pairs.

Similarly, RNA sequences, reverse sequences, complementary sequences, antisense sequences, and the like, corresponding to the polynucleotides of the present invention, may be routinely ascertained and obtained using the cDNA sequences identified as SEQ ID NO: 1-10, 21-29 and 39-46.

The polynucleotides identified as SEQ ID NO: 1-10, 21-29 and 39-46 may contain open reading frames ("ORFs") or partial open reading frames encoding polypeptides. Open reading frames may be identified using techniques that are well known in the art. These techniques include, for example, analysis for the location of known start and stop codons, most likely

5 reading frame identification based on codon frequencies, etc. Suitable tools and software for ORF analysis are available, for example, on the Internet at <http://www.ncbi.nlm.nih.gov/gorf/gorf.html>. Open reading frames and portions of open reading frames may be identified in the polynucleotides of the present invention. Once a partial open reading frame is identified, the polynucleotide may be extended in the area of the partial open
10 reading frame using techniques that are well known in the art until the polynucleotide for the full open reading frame is identified. Thus, open reading frames encoding polypeptides may be identified using the polynucleotides of the present invention.

Once open reading frames are identified in the polynucleotides of the present invention, the open reading frames may be isolated and/or synthesized. Expressible genetic constructs
15 comprising the open reading frames and suitable promoters, initiators, terminators, etc., which are well known in the art, may then be constructed. Such genetic constructs may be introduced into a host cell to express the polypeptide encoded by the open reading frame. Suitable host cells may include various prokaryotic and eukaryotic cells, including plant cells, mammalian cells, bacterial cells, algae and the like.

20 In another aspect, the present invention provides isolated polypeptides encoded, or partially encoded, by the above polynucleotides. The term "polypeptide", as used herein, encompasses amino acid chains of any length including full length proteins, wherein amino acid residues are linked by covalent peptide bonds. Polypeptides of the present invention may be naturally purified products, or may be produced partially or wholly using recombinant
25 techniques. The term "polypeptide encoded by a polynucleotide" as used herein, includes polypeptides encoded by a nucleotide sequence which includes the partial isolated DNA sequences of the present invention. In specific embodiments, the inventive polypeptides comprise an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 11-20, 30-38, 47-53 and variants of such sequences.

30 Polypeptides encoded by the polynucleotides of the present invention may be expressed and used in various assays to determine their biological activity. Such polypeptides may be used to raise antibodies, to isolate corresponding interacting proteins or other compounds, and to quantitatively determine levels of interacting proteins or other compounds.

All of the polynucleotides and polypeptides described herein are isolated and purified, as
35 those terms are commonly used in the art. Preferably, the polypeptides and polynucleotides are at

5 least about 80% pure, more preferably at least about 90% pure, and most preferably at least about 99% pure.

As used herein, the term "variant" comprehends nucleotide or amino acid sequences different from the specifically identified sequences, wherein one or more nucleotides or amino acid residues is deleted, substituted, or added. Variants may be naturally occurring allelic
10 variants, or non-naturally occurring variants. Variant sequences (polynucleotide or polypeptide) preferably exhibit at least 50%, more preferably at least 75%, and most preferably at least 90% identity to a sequence of the present invention. The percentage identity is determined by aligning the two sequences to be compared, determining the number of identical residues in the aligned portion, dividing that number by the total length of the inventive, or queried, sequence
15 and multiplying the result by 100.

Polynucleotide or polypeptide sequences may be aligned, and percentage of identical residues in a specified region may be determined against another polynucleotide, using computer algorithms that are publicly available. Two exemplary algorithms for aligning and identifying the similarity of polynucleotide sequences are the BLASTN and FASTA algorithms.
20 Polynucleotides may also be analyzed using the BLASTX algorithm, which compares the six-frame conceptual translation products of a nucleotide query sequence (both strands) against a protein sequence database. The similarity of polypeptide sequences may be examined using the BLASTP or FASTX algorithms. Both the BLASTN and BLASTP software are available on the NCBI anonymous FTP server (<ftp://ncbi.nlm.nih.gov>) under `/blast/executables/`. The BLASTN
25 algorithm version 2.0.6 [Sept-16-1998], set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of variants according to the present invention. The use of the BLAST family of algorithms, including BLASTN and BLASTP, is described at NCBI's website at URL <http://www.ncbi.nlm.nih.gov/BLAST/newblast.html> and in the publication of Altschul *et al.*,
30 "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", *Nucleic Acids Res.* 25:3389-3402, 1997. The computer algorithm FASTA is available on the Internet at the ftp site <ftp://ftp.virginia.edu/pub/fasta/>. Version 3.1t11, August 1998, set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of variants according to the present invention. The use of
35 the FASTA algorithm is described in Pearson and Lipman, "Improved Tools for Biological

- 5 Sequence Analysis," *Proc. Natl. Acad. Sci. USA* 85:2444-2448, 1988 and Pearson, "Rapid and Sensitive Sequence Comparison with FASTP and FASTA," *Methods in Enzymol.* 183:63-98, 1990. The use of the FASTX algorithm is described in Pearson *et al.*, "Comparison of DNA sequences with protein sequences," *Genomics* 46:24-36, 1997.

The following running parameters are preferred for determination of alignments and
 10 similarities using BLASTN that contribute to the E values and percentage identity: Unix running command: `blastall -p blastn -d embldb -e 10 -G 0 -E 0 -r 1 -v 30 -b 30 -i queryseq -o results;` and parameter default values:

- p Program Name [String]
- d Database [String]
- 15 -e Expectation value (E) [Real]
- G Cost to open a gap (zero invokes default behavior) [Integer]
- E Cost to extend a gap (zero invokes default behavior) [Integer]
- r Reward for a nucleotide match (BLAST only) [Integer]
- v Number of one-line descriptions (V) [Integer]
- 20 -b Number of alignments to show (B) [Integer]
- i Query File [File In]
- o BLAST report Output File [File Out] Optional

For BLASTP the following running parameters are preferred: `blastall -p blastp -d swissprot -e 10 -G 0 -E 0 -v 30 -b 30 -i queryseq -o results`

- 25 -p Program Name [String]
- d Database [String]
- e Expectation value (E) [Real]
- G Cost to open a gap (zero invokes default behavior) [Integer]
- E Cost to extend a gap (zero invokes default behavior) [Integer]
- 30 -v Number of one-line descriptions (v) [Integer]
- b Number of alignments to show (b) [Integer]
- I Query File [File In]
- o BLAST report Output File [File Out] Optional

The "hits" to one or more database sequences by a queried sequence produced by
 35 BLASTN, BLASTP, FASTA, or a similar algorithm, align and identify similar portions of

5 sequences. The hits are arranged in order of the degree of similarity and the length of sequence overlap. Hits to a database sequence generally represent an overlap over only a fraction of the sequence length of the queried sequence.

The BLASTN and FASTA algorithms also produce "Expect" values for alignments. The Expect value (E) indicates the number of hits one can "expect" to see over a certain number of
10 contiguous sequences by chance when searching a database of a certain size. The Expect value is used as a significance threshold for determining whether the hit to a database, such as the preferred EMBL database, indicates true similarity. For example, an E value of 0.1 assigned to a hit is interpreted as meaning that in a database of the size of the EMBL database, one might expect to see 0.1 matches over the aligned portion of the sequence with a similar score simply by
15 chance. By this criterion, the aligned and matched portions of the sequences then have a probability of 90% of being the same. For sequences having an E value of 0.01 or less over aligned and matched portions, the probability of finding a match by chance in the EMBL database is 1% or less using the BLASTN or FASTA algorithm.

According to one embodiment, "variant" polynucleotides, with reference to each of the
20 polynucleotides of the present invention, preferably comprise sequences having the same number or fewer nucleic acids than each of the polynucleotides of the present invention and producing an E value of 0.01 or less when compared to the polynucleotide of the present invention. That is, a variant polynucleotide is any sequence that has at least a 99% probability of being the same as the polynucleotide of the present invention, measured as having an E value of 0.01 or less using
25 the BLASTN or FASTA algorithms set at the default parameters. According to a preferred embodiment, a variant polynucleotide is a sequence having the same number or fewer nucleic acids than a polynucleotide of the present invention that has at least a 99% probability of being the same as the polynucleotide of the present invention, measured as having an E value of 0.01 or less using the BLASTN or FASTA algorithms set at the default parameters.

30 Alternatively, variant polynucleotide sequences hybridize to the recited polynucleotide sequence under stringent conditions. As used herein, "stringent conditions" refers to prewashing in a solution of 6X SSC, 0.2% SDS; hybridizing at 65°C, 6X SSC, 0.2% SDS overnight; followed by two washes of 30 minutes each in 1X SSC, 0.1% SDS at 65 °C and two washes of 30 minutes each in 0.2X SSC, 0.1% SDS at 65 °C.

5 The present invention also encompasses polynucleotides that differ from the disclosed sequences but that, as a consequence of the degeneracy of the genetic code, encode a polypeptide which is the same as that encoded by a polynucleotide of the present invention. Thus, polynucleotides comprising sequences that differ from the polynucleotide sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46, or complements, reverse sequences, or reverse
10 complements thereof, as a result of conservative substitutions are contemplated by and encompassed within the present invention. Additionally, polynucleotides comprising sequences that differ from the polynucleotide sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46, or complements, reverse complements or reverse sequences thereof, as a result of deletions and/or insertions totaling less than 10% of the total sequence length are also contemplated by and
15 encompassed within the present invention. Similarly, polypeptides comprising sequences that differ from the polypeptide sequences provided in SEQ ID NO: 11-20, 30-38 and 47-53, as a result of amino acid substitutions, insertions, and/or deletions totaling less than 10% of the total sequence length are contemplated by and encompassed within the present invention.

 Polynucleotides of the present invention also comprehend polynucleotides comprising at least a specified number of contiguous residues (*x*-mers) of any of the polynucleotides identified as SEQ ID NO: 1-10, 21-29 and 39-46, complements, reverse sequences, and reverse
20 complements of such sequences, and their variants. Similarly, polypeptides of the present invention comprehend polypeptides comprising at least a specified number of contiguous residues (*x*-mers) of any of the polypeptides identified as SEQ ID NO: 11-20, 30-38 and 47-53, and their variants. As used herein, the term "*x*-mer," with reference to a specific value of "*x*,"
25 refers to a sequence comprising at least a specified number ("*x*") of contiguous residues of any of the polynucleotides identified as SEQ ID NO: 1-10, 21-29 and 39-46, or the polypeptides identified as SEQ ID NO: 11-20, 30-38 and 47-53. According to preferred embodiments, the value of *x* is preferably at least 20, more preferably at least 40, more preferably yet at least 60,
30 and most preferably at least 80. Thus, polynucleotides and polypeptides of the present invention comprise a 20-mer, a 40-mer, a 60-mer, an 80-mer, a 100-mer, a 120-mer, a 150-mer, a 180-mer, a 220-mer, a 250-mer, a 300-mer, 400-mer, 500-mer or 600-mer of a polynucleotide or polypeptide identified as SEQ ID NO: 1-53, and variants thereof.

 The inventive polynucleotides may be isolated by high throughput sequencing of cDNA
35 libraries prepared from lymph node stromal cells of *fsn* ^{-/-} mice as described below in Example

5 1. Alternatively, oligonucleotide probes based on the sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46 can be synthesized and used to identify positive clones in either cDNA or genomic DNA libraries from lymph node stromal cells of *fsn* ^{-/-} mice by means of hybridization or polymerase chain reaction (PCR) techniques. Probes can be shorter than the sequences provided herein but should be at least about 10, preferably at least about 15 and most preferably
10 at least about 20 nucleotides in length. Hybridization and PCR techniques suitable for use with such oligonucleotide probes are well known in the art (see, for example, Mullis *et al.*, *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989; Sambrook *et al.*, *Molecular cloning -a laboratory manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989). Positive clones may be analyzed by
15 restriction enzyme digestion, DNA sequencing or the like.

The polynucleotides of the present invention may alternatively be synthesized using techniques that are well known in the art. The polynucleotides may be synthesized, for example, using automated oligonucleotide synthesizers (*e.g.*, Beckman Oligo 1000M DNA Synthesizer) to obtain polynucleotide segments of up to 50 or more nucleic acids. A plurality of such
20 polynucleotide segments may then be ligated using standard DNA manipulation techniques that are well known in the art of molecular biology. One conventional and exemplary polynucleotide synthesis technique involves synthesis of a single stranded polynucleotide segment having, for example, 80 nucleic acids, and hybridizing that segment to a synthesized complementary 85 nucleic acid segment to produce a 5 nucleotide overhang. The next segment may then be
25 synthesized in a similar fashion, with a 5 nucleotide overhang on the opposite strand. The "sticky" ends ensure proper ligation when the two portions are hybridized. In this way, a complete polynucleotide of the present invention may be synthesized entirely *in vitro*.

Polypeptides of the present invention may be produced recombinantly by inserting a DNA sequence that encodes the polypeptide into an expression vector and expressing the
30 polypeptide in an appropriate host. Any of a variety of expression vectors known to those of ordinary skill in the art may be employed. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, insect, yeast or a
35 mammalian cell line such as COS or CHO. The DNA sequences expressed in this manner may

- 5 encode naturally occurring polypeptides, portions of naturally occurring polypeptides, or other variants thereof.

In a related aspect, polypeptides are provided that comprise at least a functional portion of a polypeptide having an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 11-20, 30-38 and 47-53 and variants thereof. As used herein, the
10 "functional portion" of a polypeptide is that portion which contains the active site essential for affecting the function of the polypeptide, for example, the portion of the molecule that is capable of binding one or more reactants. The active site may be made up of separate portions present on one or more polypeptide chains and will generally exhibit high binding affinity. Such functional portions generally comprise at least about 5 amino acid residues, more preferably at least about
15 10, and most preferably at least about 20 amino acid residues. Functional portions of the inventive polypeptides may be identified by first preparing fragments of the polypeptide, by either chemical or enzymatic digestion of the polypeptide or mutation analysis of the polynucleotide that encodes for the polypeptide, and subsequently expressing the resultant mutant polypeptides. The polypeptide fragments or mutant polypeptides are then tested to
20 determine which portions retain the biological activity of the full-length polypeptide.

Portions and other variants of the inventive polypeptides may be generated by synthetic or recombinant means. Synthetic polypeptides having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may be generated using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any
25 of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain (Merrifield, *J. Am. Chem. Soc.* 85:2149-2154, 1963). Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems, Inc. (Foster City, CA), and may be operated according to the manufacturer's
30 instructions. Variants of a native polypeptide may be prepared using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see, for example, Kunkel, *Proc. Natl. Acad. Sci. USA* 82:488-492, 1985). Sections of DNA sequence may also be removed using standard techniques to permit preparation of truncated polypeptides.

Since the polynucleotide sequences of the present invention have been derived from *f5n* -
35 /- mouse lymph node stromal cells, they likely encode proteins that have important role(s) in

5 growth and development of the immune system, and in responses of the immune system to tissue injury and inflammation as well as other disease states. Some of the polynucleotides contain sequences that code for signal sequences, or transmembrane domains, which identify the protein products as secreted molecules or receptors. Such protein products are likely to be growth factors, cytokines, or their cognate receptors. The polypeptide sequence of SEQ ID NO: 13 has
10 more than 25% identity to known members of the tumour necrosis factor (TNF) receptor family of proteins, with the polypeptides of SEQ ID NO: 30, 31, 32 and 33 having more than 25% identity to known members of the fibroblast growth factor (FGF) receptor family of proteins, and the polypeptide of SEQ ID NO: 38 having more than 25% identity to known members of the WDNM1 family of proteins. These inventive polypeptides are thus likely to have similar
15 biological functions.

In particular, the inventive polypeptides may have important roles in processes such as: modulation of immune responses; differentiation of precursor immune cells into specialized cell types; cell migration; cell proliferation and cell-cell interaction. The polypeptides may be important in the defence of the body against infectious agents, and thus be of importance in
20 maintaining a disease-free environment. These polypeptides may act as modulators of skin cells, especially since immune cells are known to infiltrate skin during tissue insult, causing growth and differentiation of skin cells. In addition, these proteins may be immunologically active, making them important therapeutic targets in a large range of disease states.

In one aspect, the present invention provides methods for using one or more of the
25 inventive polypeptides or polynucleotides to treat disorders in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human.

In this aspect, the polypeptide or polynucleotide is generally present within a pharmaceutical composition or a vaccine. Pharmaceutical compositions may comprise one or more polypeptides, each of which may contain one or more of the above sequences (or variants thereof), and a physiologically acceptable carrier. Vaccines may comprise one or more of the
30 above polypeptides and a non-specific immune response amplifier, such as an adjuvant or a liposome, into which the polypeptide is incorporated.

Alternatively, a vaccine or pharmaceutical composition of the present invention may contain DNA encoding one or more polypeptides as described above, such that the polypeptide is
35 generated *in situ*. In such vaccines and pharmaceutical compositions, the DNA may be present

5 within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, and bacterial and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminator signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus Calmette-Guerin*) that expresses an immunogenic
10 portion of the polypeptide on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other poxvirus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic, or defective, replication competent virus. Techniques for incorporating DNA into such expression systems are well known in the art. The DNA may also be "naked," as described, for example, in Ulmer *et al.*, *Science*
15 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

Routes and frequency of administration, as well as dosage, will vary from individual to individual. In general, the pharmaceutical compositions and vaccines may be administered by
20 injection (*e.g.*, intradermal, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. In general, the amount of polypeptide present in a dose (or produced *in situ* by the DNA in a dose) ranges from about 1 pg to about 100 mg per kg of host, typically from about 10 pg to about 1 mg per kg of host, and preferably from about 100 pg to about 1 µg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from
25 about 0.1 ml to about 2 ml.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a lipid, a wax or a buffer. For oral
30 administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (*e.g.*, polylactic galactide) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and
35 5,075,109.

5 Any of a variety of adjuvants may be employed in the vaccines derived from this invention to non-specifically enhance the immune response. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a non-specific stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *M. tuberculosis*. Suitable adjuvants are commercially available as, for example, Freund's
10 Incomplete Adjuvant and Freund's Complete Adjuvant (Difco Laboratories, Detroit, MI), and Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ). Other suitable adjuvants include alum, biodegradable microspheres, monophosphoryl lipid A and Quil A.

The polynucleotides of the present invention may also be used as markers for tissue, as chromosome markers or tags, in the identification of genetic disorders, and for the design of
15 oligonucleotides for examination of expression patterns using techniques well known in the art, such as the microarray technology available from Synteni (Palo Alto, CA). Partial polynucleotide sequences disclosed herein may be employed to obtain full length genes by, for example, screening of DNA expression libraries, and to isolate homologous DNA sequences from other species using hybridization probes or PCR primers based on the inventive sequences.

20 The isolated polynucleotides of the present invention also have utility in genome mapping, in physical mapping, and in positional cloning of genes. As detailed below, the polynucleotide sequences identified as SEQ ID NO: 1-10, 21-29 and 39-46, and their variants, may be used to design oligonucleotide probes and primers. Oligonucleotide probes designed using the polynucleotides of the present invention may be used to detect the presence and
25 examine the expression patterns of genes in any organism having sufficiently similar DNA and RNA sequences in their cells using techniques that are well known in the art, such as slot blot DNA hybridization techniques. Oligonucleotide primers designed using the polynucleotides of the present invention may be used for PCR amplifications. Oligonucleotide probes and primers designed using the polynucleotides of the present invention may also be used in connection with
30 various microarray technologies, including the microarray technology of Synteni (Palo Alto, California).

As used herein, the term "oligonucleotide" refers to a relatively short segment of a polynucleotide sequence, generally comprising between 6 and 60 nucleotides, and comprehends both probes for use in hybridization assays and primers for use in the amplification of DNA by
35 polymerase chain reaction. An oligonucleotide probe or primer is described as "corresponding

5 to" a polynucleotide of the present invention, including one of the sequences set out as SEQ ID NO: 1-10, 21-29 and 39-46, or a variant thereof, if the oligonucleotide probe or primer, or its complement, is contained within one of the sequences set out as SEQ ID NO: 1-10, 21-29 and 39-46, or a variant of one of the specified sequences. Oligonucleotide probes and primers of the present invention are substantially complementary to a polynucleotide disclosed herein.

10 Two single stranded sequences are said to be substantially complementary when the nucleotides of one strand, optimally aligned and compared, with the appropriate nucleotide insertions and/or deletions, pair with at least 80%, preferably at least 90% to 95% and more preferably at least 98% to 100% of the nucleotides of the other strand. Alternatively, substantial complementarity exists when a first DNA strand will selectively hybridize to a second DNA
15 strand under stringent hybridization conditions. Stringent hybridization conditions for determining complementarity include salt conditions of less than about 1 M, more usually less than about 500 mM, and preferably less than about 200 mM. Hybridization temperatures can be as low as 5°C, but are generally greater than about 22°C, more preferably greater than about 30°C, and most preferably greater than about 37°C. Longer DNA fragments may require higher
20 hybridization temperatures for specific hybridization. Since the stringency of hybridization may be affected by other factors such as probe composition, presence of organic solvents and extent of base mismatching, the combination of parameters is more important than the absolute measure of any one alone.

In specific embodiments, the oligonucleotide probes and/or primers comprise at least
25 about 6 contiguous residues, more preferably at least about 10 contiguous residues, and most preferably at least about 20 contiguous residues complementary to a polynucleotide sequence of the present invention. Probes and primers of the present invention may be from about 8 to 100 base pairs in length or, preferably from about 10 to 50 base pairs in length or, more preferably from about 15 to 40 base pairs in length. The probes can be easily selected using procedures
30 well known in the art, taking into account DNA-DNA hybridization stringencies, annealing and melting temperatures, and potential for formation of loops and other factors, which are well known in the art. Tools and software suitable for designing probes, and especially suitable for designing PCR primers, are available on the Internet, for example, at URL <http://www.horizonpress.com/pcr/>. Preferred techniques for designing PCR primers are also

5 disclosed in Dieffenbach, CW and Dyksler, GS. *PCR Primer: a laboratory manual*, CSHL Press: Cold Spring Harbor, NY, 1995.

A plurality of oligonucleotide probes or primers corresponding to a polynucleotide of the present invention may be provided in a kit form. Such kits generally comprise multiple DNA or oligonucleotide probes, each probe being specific for a polynucleotide sequence. Kits of the
10 present invention may comprise one or more probes or primers corresponding to a polynucleotide of the present invention, including a polynucleotide sequence identified in SEQ ID NO: 1-10, 21-29 and 39-46.

In one embodiment useful for high-throughput assays, the oligonucleotide probe kits of the present invention comprise multiple probes in an array format, wherein each probe is
15 immobilized at a predefined, spatially addressable location on the surface of a solid substrate. Array formats which may be usefully employed in the present invention are disclosed, for example, in U.S. Patents No. 5,412,087 and 5,545,451, and PCT Publication No. WO 95/00450, the disclosures of which are hereby incorporated by reference.

The polynucleotides of the present invention may also be used to tag or identify an
20 organism or reproductive material therefrom. Such tagging may be accomplished, for example, by stably introducing a non-disruptive non-functional heterologous polynucleotide identifier into an organism, the polynucleotide comprising one of the polynucleotides of the present invention.

The polypeptides provided by the present invention may additionally be used in assays to determine biological activity, to raise antibodies, to isolate corresponding ligands or receptors, in
25 assays to quantify levels of protein or cognate corresponding ligand or receptor, as anti-inflammatory agents, and in compositions for the treatment of diseases of skin, connective tissue and the immune system.

Example 1

30 ISOLATION OF cDNA SEQUENCES FROM LYMPH NODE STROMAL CELL EXPRESSION LIBRARIES

The cDNA sequences of the present invention were obtained by high-throughput sequencing of cDNA expression libraries constructed from rodent *fsn* ^{-/-} lymph node stromal cells as described below.

35

5 *cDNA Libraries from Lymph Node Stromal Cells (MLSA and MLSE)*

Lymph nodes were removed from flaky skin *fsn* ^{-/-} mice, the cells dissociated and the resulting single cell suspension placed in culture. After four passages, the cells were harvested. Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, MD), was used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene, La Jolla, CA),
10 according to the manufacturer's specifications. A cDNA expression library (referred to as the MLSA library) was then prepared from the mRNA by Reverse Transcriptase synthesis using a Lambda ZAP Express cDNA library synthesis kit (Stratagene, La Jolla, CA). A second cDNA expression library, referred to as the MLSE library, was prepared exactly as above except that the cDNA was inserted into the mammalian expression vector pcDNA3 (Invitrogen, Carlsbad
15 CA).

The nucleotide sequence of the cDNA clone isolated from the MLSE library is given in SEQ ID NO: 1, with the corresponding amino acid sequence being provided in SEQ ID NO: 11. The nucleotide sequences of the cDNA clones isolated from the MLSA library are given in SEQ ID NO: 2-10, 21-23 and 28, with the corresponding amino acid sequences being provided in
20 SEQ ID NO: 12-20, 30-32 and 37, respectively.

Subtracted cDNA Library from flaky skin Lymph Node Stromal Cells (MLSS)

Stromal cells from flaky skin mice lymph nodes and 3T3 fibroblasts were grown in culture and the total RNA extracted from these cells using established protocols. Total RNA
25 from both populations was isolated using TRIzol Reagent (Gibco BRL Life Technologies, Gaithersburg, MD) and used to obtain mRNA using either a Poly (A) Quik mRNA isolation kit (Stratagene, La Jolla, CA) or Quick Prep^(R) Micro mRNA purification kit (Pharmacia, Uppsala, Sweden). Double-stranded cDNA from flaky skin lymph node stromal cell mRNA was prepared by Reverse Transcriptase synthesis using a lambda ZAP cDNA library synthesis kit (Stratagene)
30 that had been ligated with *Eco*RI adaptors and digested with *Xho*I to produce double-stranded fragments with *Eco*RI and *Xho*I overhanging ends.

Double-stranded cDNA from 3T3 fibroblasts was prepared using the Superscript II reverse transcriptase (Gibco BRL Life Technologies) followed by treatment with DNA polymerase I and RNaseH (Gibco BRL Life Technologies). Double-stranded 3T3 cDNA was
35 then digested with restriction endonucleases *Alu*I and *Rsa*I (Gibco BRL Life Technologies) to

5 produce blunt-ended fragments. A 20-fold excess of *AluI* /*RsaI*-digested 3T3 cDNA was hybridized with the *EcoRI/XhoI* flaky skin lymph node stromal cell cDNA in the following hybridisation solution: 50% formamide, 5xSSC, 10mM NaH₂PO₄ pH7.5, 1mM EDTA, 0.1% SDS, 200µg yeast tRNA (Boehringer Mannheim) at 37°C for 24 hours. Hybridized flaky skin lymph node stromal cell cDNA and 3T3 cDNA was then phenol/chloroform extracted and
10 ethanol precipitated. The cDNA was size-fractionated over a Sepharose CL-2B gel filtration column as described in the Lambda ZAP cDNA library synthesis protocol (Stratagene). Flaky skin lymph node stromal cell-specific cDNA was preferentially ligated into ZAP Express vector (Stratagene) by virtue of *EcoRI/XhoI* ends. Chimeric cDNA between flaky skin lymph node stromal cell cDNA and 3T3 cDNA would not be cloned due to non-compatible ends, and the
15 subtracted cDNA library was packaged using Gigapack III Gold packaging extract (Stratagene).

The nucleotide sequences of the cDNA clones isolated from the MLSS library are given in SEQ ID NO: 25-27 and 29, with the corresponding amino acid sequences being provided in SEQ ID NO: 34-36 and 38, respectively.

20

Example 2

CHARACTERIZATION OF ISOLATED CDNA SEQUENCES

The isolated cDNA sequences were compared to sequences in the EMBL DNA database using the computer algorithm BLASTN, and the corresponding predicted protein sequences (DNA translated to protein in each of 6 reading frames) were compared to sequences in the
25 SwissProt database using the computer algorithm BLASTP. Specifically, comparisons of DNA sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46 to sequences in the EMBL (Release 60, September 1999) DNA database, and amino acid sequences provided in SEQ ID NO: 11-20, 30-38 and 47-53 to sequences in the SwissProt and TrEMBL (up to October 20, 1999) databases were made as of December 31, 1999. The cDNA sequences of SEQ ID NO: 1-10, 21-24 and 27-
30 28, and their corresponding predicted amino acid sequences (SEQ ID NO: 11-20, 30-33 and 36-37, respectively) were determined to have less than 75% identity (determined as described above) to sequences in the EMBL and SwissProt databases using the computer algorithms BLASTN and BLASTP, respectively.

Isolated cDNA sequences and their corresponding predicted protein sequences, were
35 computer analyzed for the presence of signal sequences identifying secreted molecules. Isolated

5 cDNA sequences that have a signal sequence at a putative start site within the sequence are provided in SEQ ID NO: 4-6, 9-10, 25-26, 39-41 and 43-45. The isolated cDNA sequences were also computer analyzed for the presence of transmembrane domains coding for putative membrane-bound molecules. Isolated cDNA sequences that have one or more transmembrane domain(s) within the sequence are provided in SEQ ID NO: 1-3, 7, 8, 27 and 41-45.

10 Using automated search programs to screen against sequences coding for known molecules reported to be of therapeutic and/or diagnostic use, the isolated cDNA sequences of SEQ ID NO: 3, 21-24 and 29 were determined to encode predicted protein sequences that appear to be members of the tumour necrosis factor (TNF) receptor family of proteins (SEQ ID NO: 13), the fibroblast growth factor (FGF) receptor family (SEQ ID NO: 30-33) and the WDNM1
15 protein family (SEQ ID NO: 38). A family member is here defined to have at least 20% identical amino acid residues in the translated polypeptide to a known protein or member of a protein family.

As noted above, the isolated cDNA sequence of SEQ ID NO: 3 was determined to encode a predicted protein sequence (SEQ ID NO: 13) that appears to be a member of the TNF-receptor
20 family. Proteins of the TNF/NGF-receptor family are involved in the proliferation, differentiation and death of many cell types including B and T lymphocytes. Residues 18-55 of SEQ ID NO: 13 show a high degree of similarity to the Prosite motif for the TNF/NGF receptor family (Banner *et al.*, *Cell* 73:431-445, 1993). This motif contributes to the ligand binding domain of the molecule and is thus essential to its function. (Gruss and Dower, *Blood* 85:3378-
25 3404, 1995). The polypeptide of SEQ ID NO: 13 is therefore likely to influence the growth, differentiation and activation of several cell types, and may be usefully developed as an agent for the treatment of skin wounds, and the treatment and diagnosis of cancers, inflammatory diseases, and growth and developmental defects.

The isolated cDNA sequence of SEQ ID NO: 29 was determined to encode a predicted
30 protein sequence (SEQ ID NO: 38) that appears to be a member of the WDNM1 protein family. The WDNM1 family of proteins has a conserved arrangement of cysteine residues. The family includes several proteinase inhibitors, suggesting that WDNM1 could encode a product with proteinase inhibiting capacity. The WDNM1 gene has been shown to be down-regulated in metastatic rat mammary adenocarcinomas (Dear and Kefford, *Biochem. Biophys. Res. Comm.*
35 176:247-254, 1991).

5 The isolated cDNA sequence of SEQ ID NO: 21 was determined to encode a predicted protein sequence (SEQ ID NO: 30) that appears to be a member of the fibroblast growth factor (FGF) receptor family of proteins, specifically the FGF receptor 3. Fibroblast growth factor receptors belong to a family of four single membrane-spanning tyrosine kinases (FGFR1 to 4). These receptors serve as high-affinity receptors for 17 growth factors (FGF1 to 17). FGF
10 receptors have important roles in multiple biological processes, including mesoderm induction and patterning, cell growth and migration, organ formation and bone growth (Xu, *Cell Tissue Res.* 296:33-43, 1999). Further analysis of the sequence revealed the presence of a putative transmembrane domain and intracellular domain, similar to other FGF receptors.

 The isolated cDNA sequence of SEQ ID NO: 44 was determined to encode a predicted
15 protein sequence (SEQ ID NO: 52) that appears to be a lysyl oxidase-related protein. Lysyl oxidase is a copper-dependent amine oxidase that has an important role in the formation of connective tissue matrices. The molecule is involved in crosslinking of the extracellular matrix proteins, collagen and elastin (Smith-Mungo and Kagan, *Matrix Biol.* 16:387-398, 1998). Expression of lysyl oxidase is upregulated in many fibrotic diseases, and down regulated in
20 diseases involving impaired copper metabolism. Identification of new lysyl oxidase-related proteins indicates the existence of a multigene family. Experimental evidence suggests that lysyl oxidase may have other important biological functions in addition to its role in cross-linking of collagen and elastin (Smith-Mungo and Kagan, *Matrix Biol.* 16:387-398, 1998).

 The isolated cDNA sequence of SEQ ID NO: 45 was determined to encode a predicted
25 protein sequence (SEQ ID NO: 53) that appears to be a CD99-like protein. CD99, also referred to as MIC2, is a cell surface molecule involved in T cell adhesion processes (Gelin *et al.*, *EMBO J.* 8:3252-3259).

Example 3

30 ISOLATION OF FULL LENGTH cDNA SEQUENCE OF A MURINE FIBROBLAST
 GROWTH FACTOR RECEPTOR HOMOLOG

 The full-length cDNA sequence of a murine fibroblast growth factor receptor homolog was isolated as follows.

35 The MLSA cell cDNA library (described in Example 1) was screened with an [α 32 P]-

5 dCTP labeled cDNA probe corresponding to nucleotides 1 to 451 of the coding region within SEQ ID NO: 21. Plaque lifts, hybridization and screening were performed using standard molecular biology techniques. The determined polynucleotide sequence of the full-length murine FGFR gene (referred to as muFGFR- β) is provided in SEQ ID NO: 22, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 31.

10 Analysis of the polynucleotide sequence of SEQ ID NO: 22 revealed the presence of a putative transmembrane domain corresponding to nucleotides 1311 to 1370. The polypeptide sequence (SEQ ID NO: 31) has regions similar to the extracellular domain of the fibroblast growth factor receptor family.

A splice variant of SEQ ID NO: 22 was also isolated from the MLSA cDNA library as described in Example 1. The determined polynucleotide sequence of the splice variant (referred to as FGFR- γ) is provided in SEQ ID NO: 23 and the corresponding predicted amino acid sequence is provided in SEQ ID NO: 32. The splice regions are in an equivalent position to splice sites for previously described FGF receptors (Ornitz, *J. Biol. Chem.* 296:15292-15297, 1996; Wilkie, *Current Biology* 5:500-507, 1995; Miki, *Proc. Natl. Acad. Sci. USA* 89:246-250, 20 1992), thus providing further evidence that this molecule is a FGF receptor homolog.

EXAMPLE 4

ISOLATION OF A HUMAN FGF RECEPTOR HOMOLOG

25 The cDNA EST encoding the partial murine FGF receptor (SEQ ID NO: 21) was used to search the EMBL database (Release 58, March 1999) to identify human EST homologs. The identified EST (Accession Number AI245701) was obtained from Research Genetics, Inc (Huntsville AL) as I.M.A.G.E. Consortium clone ID 1870593. Sequence determination of the complete insert of clone 1870593 resulted in the identification of 520 additional nucleotides. 30 The insert of this clone did not represent the full-length gene. The determined nucleotide sequence of the complete insert of clone 1870593 is given in SEQ ID NO: 24 and the corresponding predicted amino acid sequence in SEQ ID NO: 33.

EXAMPLE 5

CHARACTERIZATION OF MURINE FGF RECEPTOR HOMOLOG

5

The murine FGF receptor homolog, muFGFR- β and splice variant FGFR- γ (SEQ ID NO: 22 and 23, respectively) were expressed in mammalian cells and the purified protein used to determine the ligand binding specificity of the molecules.

10 The extracellular domains of muFGFR- β and FGFR- γ (SEQ ID NO: 22 and 23, respectively) were amplified by PCR using primers MS158 and MS159 (SEQ ID NO: 55 and 56, respectively) and cloned into the expression vector pcDNA3 containing the Fc fragment from human IgG1. These recombinant proteins, referred to as FGFR β Fc and FGFR γ Fc, were expressed in HEK293 cells (ATCC No. CRL-1573, American Type Culture Collection, Manassas, VA) and purified using an Affiprep protein A column (Biorad, Hercules CA).

15 Binding of muFGFR- β to FGF-2 (basic fibroblast growth factor) was demonstrated by co-incubating the purified protein and FGF-2 in the presence of protein G Sepharose (Amersham Pharmacia, Uppsala, Sweden) and resolving complexes formed on denaturing polyacrylamide gels. FGF-2 (2 μ g) was incubated with 5 μ g FGFR β Fc, FGF Receptor 2 (FGFR2Fc) or unrelated protein (MLSA8790Fc) in 5 μ l protein G fast flow beads (Pharmacia, Uppsala, Sweden), PBS and 0.1% Triton X-100 for 60 min at 4°C. The beads were washed three times in 0.1% Triton X-100/PBS and resuspended in 20 μ l loading buffer (0.1 M DTT, 10% sucrose, 60 mM Tris.HCl pH 6.8, 5% SDS and 0.01% bromophenol blue). The samples were analysed on a 12% polyacrylamide gel. FGF-2, FGFR2Fc, FGFR β Fc and MLSA8790Fc (1 μ g of each) were loaded on the gel for comparison. After staining of the gel with Coomassie blue, a doublet of bands were visible in the lane containing FGFR β Fc, indicating that a complex formed between the FGF-2 and the murine FGF receptor homolog FGFR β Fc, and that FGF-2 is a ligand for the novel FGF receptor homolog. A doublet was also observed in the lane containing the FGFR2Fc, which was the positive control. No doublet was observed in the negative control lane containing the MLSA8790Fc protein.

30 The binding specificity of the murine FGF receptor homolog FGFR β Fc was further examined by repeating the experiment described above, replacing the FGF-2 with another known growth factor, epidermal growth factor (EGF). In this experiment, EGF did not bind to FGFR2Fc, the FGFR β Fc or MLSA8790Fc, indicating that binding of FGF-2 to the murine FGF receptor homolog FGFR β Fc was specific.

5

EXAMPLE 6
SEQUENCE DETERMINATION OF A POLYNUCLEOTIDE FRAGMENT
CONTAINING GENOMIC MURINE FGFR β

10

Mouse genomic DNA was isolated from L929 cells using standard techniques. A genomic polynucleotide fragment containing murine FGFR β was PCR amplified using primers MS157 and MS166 (SEQ ID NO: 56 and 57, respectively). The 1.4 kb polynucleotide fragment was cloned into a T-tailed pBluescript SK²⁺ vector. The sequence of the insert of this plasmid was determined using standard primer walking sequencing techniques. The determined base sequence of the genomic fragment containing murine FGFR β is given in SEQ ID NO: 46.

15

CLAIMS:

1. An isolated polypeptide comprising a sequence selected from the group consisting of SEQ ID NO: 11-20, 30-38 and 47-53.
2. An isolated polypeptide comprising a sequence selected from the group consisting of:
 - (a) sequences having at least 40% identity to a sequence provided in SEQ ID NO: 11-20, 30-38 and 47-49, 51 and 52 as determined using the computer algorithm BLASTP;
 - (b) sequences having at least 60% identity to a sequence provided in SEQ ID NO: 11-20, 30-38 and 47-53 as determined using the computer algorithm BLASTP;
 - (c) sequences having at least 75% identity to a sequence provided in SEQ ID NO: 11-20, 30-38 and 47-53 as determined using the computer algorithm BLASTP; and
 - (d) sequences having at least 90% identity to a sequence provided in SEQ ID NO: 11-20, 30-38 and 47-53 as determined using the computer algorithm BLASTP.
3. An isolated polynucleotide that encodes a polypeptide according to any one of claims 1 and 2.
4. An isolated polynucleotide of claim 3, wherein the polynucleotide comprises a sequence selected from the group consisting of sequences provided in SEQ ID NO: 1-10, 21-29 and 39-46.
5. An isolated polynucleotide comprising a sequence selected from the group consisting of:
 - (a) complements of a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46;
 - (b) reverse complements of a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46;
 - (c) reverse sequences of a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46;
 - (d) sequences having at least 40% identity to a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46 as determined using the computer algorithm BLASTN;
 - (e) sequences having at least 60% identity to a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46 as determined using the computer algorithm BLASTN;
 - (f) sequences having at least 75% identity to a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46 as determined using the computer algorithm BLASTN; and
 - (g) sequences having at least 90% identity to a sequence provided in SEQ ID NO: 1-10, 21-29 and 39-46 as determined using the computer algorithm BLASTN.

6. An isolated polynucleotide comprising a sequence selected from the group consisting of:
(a) sequences that are a 200-mer of an isolated polynucleotide according to any one of claims 3, 4 and 5; (b) sequences that are a 100-mer of an isolated polynucleotide according to any one of claims 3, 4 and 5; and (c) sequences that are a 40-mer of an isolated polynucleotide according to any one of claims 3, 4 and 5.
7. An expression vector comprising an isolated polynucleotide according to any one of claims 3-6.
8. A host cell transformed with an expression vector according to claim 7.
9. An isolated polypeptide comprising at least a functional portion of a polypeptide having an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 11-20, 30-38 and 47-53.
10. A pharmaceutical composition comprising an isolated polypeptide according to any one of claims 1, 2 and 9.
11. A pharmaceutical composition comprising an isolated polynucleotide according to any one of claims 3-6.
12. A method for the treatment of an inflammatory disorder in a patient, comprising administering to the patient a pharmaceutical composition according to any one of claims 10 and 11.
13. A method for modulating the growth of blood vessels in a patient, comprising administering to the patient a pharmaceutical composition according to any one of claims 10 and 11.
14. A method for the treatment of a disorder of the immune system in patient, comprising administering to the patient a pharmaceutical composition according to any one of claims 10 and 11.
15. A method for the treatment of cancer in a patient, comprising administering to the patient a pharmaceutical composition according to any one of claims 10 and 11, wherein the cancer is selected from the group consisting of epithelial, lymphoid, myeloid, stromal and neuronal cancers.
16. A method for the treatment of a tumour necrosis factor-mediated disorder in a patient, comprising administering to the patient a composition comprising an isolated

polypeptide, the polypeptide comprising an amino acid sequence selected from the group consisting of:

- (a) a sequence of SEQ ID NO: 13;
 - (d) sequences having at least 40% identity to the sequence of SEQ ID NO: 13 as determined using the computer algorithm BLASTP;
 - (e) sequences having at least 60% identity to the sequence of SEQ ID NO: 13 as determined using the computer algorithm BLASTP;
 - (f) sequences having at least 75% identity to the sequence of SEQ ID NO: 13 as determined using the computer algorithm BLASTP; and
 - (d) sequences having at least 90% identity to the sequence of SEQ ID NO: 13 as determined using the computer algorithm BLASTP.
17. The method of claim 16, wherein the tumour necrosis factor-mediated disorder is selected from the group consisting of arthritis, inflammatory bowel disease and cardiac failure.
18. A method for the treatment of a viral disorder in a patient, comprising administering to the patient a pharmaceutical composition according to any one of claims 10 and 11.
19. The method of claim 18, wherein the viral disorder is HIV-infection.
20. A method for the treatment of a fibroblast growth factor-mediated disorder in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence selected from the group consisting of:
- (a) a sequence provided in SEQ ID NO: 30-33;
 - (b) sequences having at least 40% identity to a sequence provided in SEQ ID NO: 30-33 as determined using the computer algorithm BLASTP;
 - (c) sequences having at least 60% identity to a sequence provided in SEQ ID NO: 30-33 as determined using the computer algorithm BLASTP;
 - (d) sequences having at least 75% identity to a sequence provided in SEQ ID NO: 30-33 as determined using the computer algorithm BLASTP; and
 - (e) sequences having at least 90% identity to a sequence provided in SEQ ID NO: 30-33 as determined using the computer algorithm BLASTP.

SEQUENCE LISTING

<110> Strachan, Lorna
 Sleeman, Matthew
 Abernethy, Nevin
 Onrust, Rene
 Kumble, Anand
 Murison, Greg

<120> Compositions isolated from stromal cells
 and methods for their use.

<130> 1037C1PCT

<160> 57

<170> FastSEQ for Windows Version 3.0

<210> 1

<211> 803

<212> DNA

<213> Mouse

<400> 1

```

gttctgaatg ggagcatcag ccctctctgg gctgttgccc cgacattaca ggtcctgtct
60
ctcagggaagc tgggccttgg ttctggcgct gcagagatgg acttctctgc gtttggaat
120
ctgcgggcgt tggatctgtc gggaaactcc ctgaccagct tccaaaagtt caagggcagt
180
ttggcccttc ggactctcga cctccgcaga aactctctca cggccctccc tcagagggtt
240
gtgtccgagc agcctctgag gggctctgcag accatctacc tcagccagaa cccttatgac
300
tgctgtgggg tggaaggatg gggggccctg cagcagcact tcaagactgt tgccgacttg
360
tccatgggtca cttgcaacct ctctccaag atcgctccgtg tgggtggagct gccgaaggc
420
ctgcctcagg gctgtaagtg ggaacagggtg gacactggtc tcttctacct cgtgctcatc
480
gtcccagct gcctcacct gctggtggcc tgtactgtcg tcttcctcac ttttaagaag
540
cctttgcttc aggtcatcaa gagccgctgc cactggtcct ccatatactg acccgtgtgc
600
caaggctaga gacttggttt ttctcgagg atgcgtctct ccgctggatc tttacttttg
660
caggggtcga gtgtgatgca ttgaagggtt aaactgaaat ttgaaagagt tccatcctca
720
gtcccattaa cttctcctcc catccgtgtg atttatcctc attgtcctgg tgaaatattt
780
attaaacgac attctgtgag att
803

```

<210> 2

<211> 689

<212> DNA

<213> Mouse

<400> 2

```

gtcgctgag gtccccgccg acgacgcact caccatggcg cctgctaacc ttgggtgac
60
gccgcactgg gtgatgctcc tcggtgccgt gctgctgttg cttctgtccg gagcctccgc
120

```

gcaggaacct ccgagagtgg gttgctctga gtacacaaac agatcctgtg aagagtgcct
 180
 caggaatgtc tcctgtctgt ggtgcaatga gaacaaggcg tgtatggact acccagttag
 240
 gaaaatcttg cccctgctt ctctctgtaa attgagttcc gctcgtggtg gcgtatgctg
 300
 ggtgaacttc gaggccttga tcatcaccat gtcggtcctg gggggctctg tgctcctggg
 360
 catcactgtg tgctgctgct actgctgccg ccggaagaag agccggaagc cagacaagag
 420
 cgatgagcgg gccatgagag agcaggagga gaggagagtg cggcaggagg aaaggagggc
 480
 ggaaatgaag tcaagacatg atgaaatcag gaaaaatac ggtctgttta aagaacaaaa
 540
 cccgtatgag aagttctaag gtggctggca cacacttggt gtggatcgtg cagttccaga
 600
 gtttcctggg aatgcactcc ccagcagagc ctgcagagac ctcaccacca tggccaccct
 660
 tgacctgggt gatccctcag cctctactg
 689

<210> 3
 <211> 619
 <212> DNA
 <213> Mouse

<400> 3
 ggcaccaggg aagccctgcc ggggcctgtc ccacagaacc tgcaccccca gatgccgccc
 60
 tatgcctttg ttcacccacc cttccccctg ccacctgtgc ggcccgtgtt caacaacttc
 120
 cccatcaaca tgggtcctgt gcccgctccc tatgtccccc ctctgcccac cgtgcgtgtc
 180
 aactatgact ttggccacat gcacgtgcc cttggagcaca acctgcccac gcactttggc
 240
 ccccaaccac ggcacgctt ctgacaccca aagccctgtc agccgtgccg agtctgtagg
 300
 agggcccagt ctcactttct gagtaggggt gaaggcctcc attccctctc gaaagtggag
 360
 gcgtgtcctc ctgctcttac ctttgcaagg tccatgtctc ttcaggctctg atgccctctg
 420
 ggtgctgatt gtcactgggc caattatagg gcagctccct agtctgccat cttagcagcc
 480
 aatccagtgg ccctgaccat gaagcaaggc ctctaactgt ttgccatact tcctccccag
 540
 cagcccaatg aaagcccagg gggaaatggc ctaccatccc taagccaggg ctctctcctt
 600
 gttgcccag gccactta
 619

<210> 4
 <211> 1630
 <212> DNA
 <213> Mouse

<400> 4
 ggcgcgtgag cctcaggatg aacctgtgtt ttctagcgg gctgtatggc tctcggtttt
 60
 tctcaacgct cccgtatggt ggccgcgggt gccggggtga cccggctgct agtgctcttg
 120
 ctgatggtag ccgcggctcc tagcagagcc cgaggcagcg gctgccgggt cggggcctcc
 180
 gcgcgtggga ccggggccga tggccgtgaa gctgagggct gtggcaccgt ggctttgctg
 240
 ctggagcatt catttgagct cggatgatga gccaaacttc agaagcgagg cttgctgctc
 300

tgggaaccagc aggatggcac cctgtcggca acacagcgac agctcagtga ggaggagcgt
 360
 ggccgactcc gggatgtggc tgcgtgcaat ggccctctaca ggggtccgggt cccgaggcgg
 420
 cctgggacac ttgatgggtc agaagctggc ggccatgtgt ctcccttcgt cccagcgtgc
 480
 tccctgggtg agtcgcacct ttcggaccag ctgaccttgc acgtggatgt ggctggcaac
 540
 gtgggtgggc tgtctgtggt ggtgtaccct gggggctgcc ggggctccga ggtggaagat
 600
 gaggacctgg agctgttcaa tacatctgtg cagctgcggc ctcccagcac tgctccaggc
 660
 cccgagactg cagccttcat tgagcgctg gagatggagc agggccagaa ggccaagaac
 720
 ccacaggagc agaagtcttt ctttgccaaa tactggatgt acatcattcc agttgtgctg
 780
 ttctcatga tgcggggagc gccggacgct gggggccagg gcggcggtgg gggcgggggc
 840
 agcagccggt gagcagctgt gccacctaga gccccccca gagccagccc aagaaggagt
 900
 tcctgacccc acatttccct attgcatgaa tatggaaggc tgtcccttca gtgagccctc
 960
 tggccttct gtaagcccct ctttctgtcc ctgagcctct ctctcatcct gttgactgag
 1020
 agcttgggtg gacctccctg tagccagctc actgcaactg tgccccacca tgtggcactg
 1080
 tgctcctctg tctgctaaac acccaccagc ctgccccacc ccaccccacc atacactttg
 1140
 ggaacttgcc aagctctctc cagcctctgt gcctttgcc tgcaggcccc gtgcgcccct
 1200
 cactgtcact ctccagccct ttgccaaagga tctgtggccc agaggcctct gctcttagtg
 1260
 gctaggtcag cctccagccc actgtccagg tggcatgctg tcttctttgc cccctctct
 1320
 ggtgccccag aataccatgg tgacctacca ctatccttct tgcccttggga tgtcatagcc
 1380
 tggatctgtc accaggagag gattgtgggc ctccacgtta gtctgtgaat gcacacttgc
 1440
 agtgacttgt gtgcaggttt tgagagccgg ttttgacta gctgctcgac agctgctggc
 1500
 atggccgtgc tcttgacat gcgcgcgtgt gggcatgggg attgctgtgc agcctcagct
 1560
 gtgttgtgtg gctgctgatt aaactgtccc ctaaacagca aaaaaaaaaa aaaaaaaaaa
 1620
 aaaaaaaaaa
 1630

<210> 5
 <211> 1197
 <212> DNA
 <213> Mouse

<400> 5

ggcaccagac gactggggcc ctaccccatg tggacaacct caccatgcgt ctggaccccg
 60
 gtgtggggcg ctcagtata ggcgtagtga cagtgcagc gacagctaga gggatgatag
 120
 acccccaaac tagtgactt tgaagtttct tcccagccg gttccagcct cctggaacaa
 180
 ccattgtgcc agttttgcgc gtgccaaatt caggcgctg cccaagcggg gctgctatct
 240
 gaattctcct tggatgtggc aaagggaat gaacgcaaaa ggtgccgctg gaagtgtccg
 300
 acctagagaa atatgtagac cggagccctg ttaccttctt ccagcatgga ctctctgggt
 360
 ctcttcttgt tctacttggc cttcttattg atttgtgttg tctgatctg catcttcaca

420
 aaaagccagc gtttgaaggc cgtggtcctt ggaggagcac aggtagcact ggtccttggg
 480
 tactgcccg atgtgaatac tgtgttaggt gctagtctgg aaggctcaca agacaagggg
 540
 atgtgagtct tgtctttaat cctggcactt gggaggctga ggcttcgggg ccagttgggg
 600
 ctacatcgca agagcctgtg tccaaacaaa caaacggtg tctttttgct ttgagatagg
 660
 tcgaataggt cgaattttca aggttggtt tttaaacagt gtgtaatgtc tgtatttggg
 720
 tgtgactcct gtttgccatg acatgcttgt agcaggtgtg aactcaggag gacacaagtg
 780
 accagaaagc tgagcatcta gctgtcaatc ttcccttcac attgtcccat ctgtcttccc
 840
 ttgggggtca aagcaaagtg ggggcaagta gccacgaagg ggttgacttg ggaggacct
 900
 ggggatctgg aggccaatct tgagcatgga gcagacctga gggtaggga agcccacgtc
 960
 cacagcagcc tctgcacacc ccttttcccc acagactcca acagacacat tctgtgcagt
 1020
 caaggtagaa atggaggtgt tctctacacc tcctaaatcc tagcacttag gaagctgagg
 1080
 caggattatg aattccaggc tagctcgggt tatgtaatga gactgtttca aacacagagc
 1140
 ggagccgagg agatggctgg gcagtcacag agctgccgtg caaccagaac tggaggg
 1197

<210> 6
 <211> 1435
 <212> DNA
 <213> Mouse

<400> 6
 catgggcgcc gtctggtcag cctgctggt cggcgggggt ctagctggag cgctcatcct
 60
 gtggctgctg cggggagact ctggggcccc ggggaaagac ggggttgagg agccgccgca
 120
 gaaggcgca cctcctgggg aggctgcggc cccgggagac ggtccgggtg gtggtggcag
 180
 tggcgccctg agccctgaac cttccgatcg ggagctggtc tccaaagcag agcatcttcg
 240
 agaaagcaac ggacatttga tttctgagag caaagatctt ggtaacctgc cggaagcaca
 300
 gcggctgcag aatgttggag cagactgggt caatgccaga gagtttgttc ctgttgggaa
 360
 gattccagac acacactcca gggccgactc tgaagcggca agaaatcaaa gcccaggatc
 420
 tcatggagga gaatggagac tccccaaagg acaagaaaca gctgtcaaag tagctggcag
 480
 tgtggccgca aagctggcct ccagcagcct gcttggggac agagctaaag cagtcagtca
 540
 ggaccaggca ggccacgagg actgggaagt ggtgtctagg cactcatctt gggggagtgt
 600
 tggtttgggt ggcagtcttg aggcttctag gttaagtcta aatcagagaa tggacgacag
 660
 caaaaacagt cttgtgggag gaagaggctg ggaagtagat gggaaagtgg catctctgaa
 720
 acctcaacag gtcagcatcc agttccagggt gcactacacc acaaacaccg atgtgcagtt
 780
 cattgcagtg actggagacc atgagagcct tgggagatgg aacacatata tccactcca
 840
 ctactgcaaa gacgggctct ggtctcattc tgtcttcctg cctgcagaca cagtgggtga
 900
 gtggaagtgc gtgttggtag agaataagga agttactcgt tgggaagaat gcagcaatag
 960

attcctgcag actggccatg aggataaagt ggttcatggg tggtagggga ttcactgact
 1020
 cagttttcag agcatccaag aggctgcagc agaattgtga caaggctaag gcttttagagc
 1080
 gcaactgcata gcttaaagta aaggcgggtg gattccaatt gtagccatca gggctctttc
 1140
 agatttgcta gtgtggcttt tgtccaaaat gtaggaagat gtatgcctgc agataatgct
 1200
 tcctgtaanc tggcacttgt cccttattgt attgactggg ttgtgctgac acatcaggac
 1260
 ttgaggaatt gatcatcctg ggtagttgca tcttgggtag tacacctgag gtatggacta
 1320
 catatgggca aggagcaact aagcaactgc acgggtacaa ggtagagcgc ccttagcagc
 1380
 tcttagacta gaaagactac aataagcccc atcaaacaca gctaaagcaa cactg
 1435

<210> 7
 <211> 1131
 <212> DNA
 <213> Mouse

<400> 7
 ggcaccagcc cggcttctgt gctccgctca gtctccagcg atccctccct acctccgccc
 60
 tccatggcgt cgctcctgtg ctgtgggect aagctggccg cctgtggcat cgctcctcagc
 120
 gcctggggag tgatcatggt gataatgctc gggatatttt tcaatgtcca ttctgctgtg
 180
 ttaattgagg acgttccctt cacagagaaa gattttgaga acggctcctca gaacatatac
 240
 aacctgtacg agcaagtcag ctacaactgt ttcacgccc cgggcctcta cctcctcctc
 300
 ggaggcttct ccttctgcc agttcgtctc aacaagcgca aggaatacat ggtgcgctag
 360
 agcgcggtcc gcctctccct cccagcccc cttctctatt taaagactcc gcagactccg
 420
 tcccactcat ctggcgctct ttgggacttg tgaccctagc gagacgtcat ccctggccct
 480
 gcaaaaactgc gccagcctc tggaggagac cgagggtgac cgcgccccgt tctgaactac
 540
 aataaaaaga agcggttccc cctaagcttg ctgtctgtgc ttccagggag gggcgggccc
 600
 gggctggaag gggctgagac cggcctcatc gaggagtccg gaccctccga cgggaagtga
 660
 atgaagctag ccggaagtga agcaacgtct tccacctcgt cttcctccgc gcggcgaggc
 720
 cccttgagtg actggggaga ggtcgggtct cggccaatca gctgcaggga gggcgggact
 780
 ttctgcgcgg gagcccgagc ggccggctgc cgggctctcc gtggtttcca gctcgcgtgg
 840
 tggtaggtgg ggcggagcgt ctccgtgagg aggtgcgcgg ggccatgacg tcagcgtcca
 900
 ccaaggttgg agagatcttc tccgcgccg gcgcgcctt cacgaagctc ggggagttga
 960
 cgatgcagct gcatccagtc tcggactctt cccctgccgg tgccaagtgg acggagacgg
 1020
 agatagagat gctgagggt gctgtgaagc gctttgggga cgatcttaat cacatcagct
 1080
 gtgtcatcaa ggaacggaca gtggctcaga taaagaccac tgtgaagcga a
 1131

<210> 8
 <211> 1357
 <212> DNA
 <213> Mouse

<400> 8

```

    gggagggcct ggagggccgag gcgggacaggc accagccaga gcagctggcg gcagacggca
60   ggcagacagt cagaccgtct agcgggcctg gcttgccctac ctggcagctg caccgggtcc
120  ttcaccaga gctggttcca tagctcaaca tggccccctg gttcctcctg tctctgtgc
180  tacttgcgag gcctgtgcct ggggtggcct actctgtgtc actcccgcc tccttcctgg
240  aggatgtagc cggcagcggg gaagctgagg gttcttcagc ctcttccccg agcctgccgc
300  cgcctgggac tccagccttc agtcccacac cggagagacc ccagcccaca gctctggacg
360  gccccgtgcc acccaccaac ctccctggaag ggatcatgga tttcttccgg cagtacgtga
420  tgctcatcgc ggtggtgggc tcgctgacct tcctcatcat gttcatagtc tgcgcggccc
480  tcatcacgcy ccagaagcac aaggccacag cctactacc atcctcgttc cctgaaaaga
540  agtatgtgga ccagagagac cgggctgggg gaccccgtag cttcagcgag gtccctgaca
600  gggcacctga cagccggcat gaagaaggcc tggacacctc ccatcagctc caggctgaca
660  ttctggctgc taccagaac ctccgggtctc cagctagagc cctgccaggc aatggggagg
720  gagcaaagcc tgtgaagggt gggtcggagg aggaggagga agaggtgctc agcggtcagg
780  aggaggccca ggaagcccca gtatgtgggg tcaactgaaga gaagctgggg gtcccagagg
840  agtcgggtctc agcagaggct gaaggggttc ctgccaccag tgagggccaa ggggaagcag
900  aagggtcttt ctcccttagcc caggaatccc agggagcaac tggctcctct gaaagtccct
960  gtgcctgcaa cagagtctcc cccagtgtct aacaggcccc agaactgctg ggacccgaat
1020 gttgggtcct tgagggtcac ctctttggtc aagaaaggca ttcagctcta actgctcctt
1080 gataccacgt ggcttggcca ttgctggtgc caaggctgac cccgaactgg cagagccgat
1140 gccctctggt gcaccccagg aaacatctcc ccaagttcca gcgcccttaa tgactcttgc
1200 caccctgggg gcttcaccct aacgcaccac ttctctggaa ggggaaggcc agacacatgc
1260 cagttggggc tgcctgaggc agtctcaga gcagaagggg accaggccag aggccacctg
1320 tgacggggca aactgcatct cggtgtgga gaccaga
1357

```

<210> 9

<211> 815

<212> DNA

<213> Mouse

<400> 9

```

    aggtcgacac tagtggatcc aaagaattcg gcacgagggg acgcggagcg gtcgcgtgcy
60   cggagagcag ctctggggcg cggggcggtg ctgcggggcg tcaggggccc tgggaacaat
120  ggcgctgtgc gcgcggggcg cgctgctgct gggcgctgct cagggtgctg cgctgctagg
180  ggcggcgag gaccgaccg acgctcaggg ctctgcaagt ggaaaccact cagtgtgac
240  ctccaatatt aacataacag agaataccaa ccagaccatg agtgtggttt ccaaccagac
300  cagtgaatg cagagcaccg cgaagccttc cgtactgcca aaaactacca cacttatcac

```


360
 tgtgaaacct gcaactattg ttaaaatata aaccccagga gtcttaccac atgtgacgcc
 420
 tactgcctca aagtctacac ccaatgcaag tgcttctcca aactctaccc acacgtcagc
 480
 atccatgaca accccagccc acagtagttt attgacaact gtaacggttt cagcaactac
 540
 tcattcccacc aaaggcaag gatccaagtt tgatgccggc agctttgttg gtggtatagg
 600
 tggttaacact gggagtttta tctattctct acattggatg caaaatgtat tattcaagaa
 660
 gaggcattcg gtaccgaagc attgacgaac atgatgccat catttaaaagt acttcagtgg
 720
 tcaaggaaag aagaaagact gcagccttat caattatatt gggttatatt agtttaaact
 780
 attattttct tggaagtagt ataaacaagt catgc
 815

<210> 10
 <211> 1129
 <212> DNA
 <213> Mouse

<400> 10
 ccaacactcg ccatgcgttc tggggcactg tggccgctgc tttggggagc cctggtctgg
 60
 acagtgggat ccgtgggcgc cgtgatgggc tccgaggatt ctgtgcccgc tggcgtgtgc
 120
 tggctccagc agggcagaga ggccacctgc agtctggtgc tgaagactcg tgtcagccgc
 180
 gagagtgct gtgcttcgcg caacatcaac accgcctggc ccaacttcac ccaccaggc
 240
 aataaaatca gcctgctagg gttcctgggc ctgctccact gcctcccctg caaagattcc
 300
 tgcgacggag tggagtgcgc ccccgcaag gcgtgccgca atgctggggg ggcgtccaac
 360
 aactgcgagt gcgtgcccac ctgcgagggg tttcccgcgc gcttcagggt ctgcggtct
 420
 gatggcgcca cctaccggga cgaatgcgaa ctgcgcaccg cgcgctgtcg cggacacca
 480
 gacttgccgc tcatgtaccg cggccgctgt caaaagtctt gcgctcagggt agtgtgccc
 540
 cgtccccagt cgtgccttgt ggatcagacc ggcagcgcac actgcgtggg gtgtcgcgct
 600
 gcgcccctgc cagtaccttc caaccgcgc caagaactct gtggcaacaa caacgttacc
 660
 tacatctcgt cgtgtcacct gcgccaggcc acttgcttcc tgggccgcct cattgggggt
 720
 cggcaccag gcatctgcac aggtggcccc aagttcctga agtctggcga tgctgccatt
 780
 gttgatattg tccctggcaa gcccatgtgt gttgagagct tctctgacta ccctccactt
 840
 ggtcgccttg ctgttcgtga catgaggcag acagttgctg tgggtgtcat caaagctgtg
 900
 gacaagaagg ctgctggagc tggcaaagtc accaagtctg cccagaaagc tcagaaggct
 960
 aaatgaatat taccctaacc acctgccacc ccagtcttaa tcagtgggtg aagaacggtc
 1020
 tcagaactgt ttgtctcaat tggccattta agtttaatag taaaagactg gttaatgata
 1080
 acaatgcata gtaaaacctt cagaaggaaa gaatgtgtg gaccatttt
 1129

<210> 11
 <211> 196
 <212> PRT

<213> Mouse

<400> 11

Val Leu Asn Gly Ser Ile Ser Pro Leu Trp Ala Val Ala Pro Thr Leu
 1 5 10 15
 Gln Val Leu Ser Leu Arg Asp Val Gly Leu Gly Ser Gly Ala Ala Glu
 20 25 30
 Met Asp Phe Ser Ala Phe Gly Asn Leu Arg Ala Leu Asp Leu Ser Gly
 35 40 45
 Asn Ser Leu Thr Ser Phe Gln Lys Phe Lys Gly Ser Leu Ala Leu Arg
 50 55 60
 Thr Leu Asp Leu Arg Arg Asn Ser Leu Thr Ala Leu Pro Gln Arg Val
 65 70 75 80
 Val Ser Glu Gln Pro Leu Arg Gly Leu Gln Thr Ile Tyr Leu Ser Gln
 85 90 95
 Asn Pro Tyr Asp Cys Cys Gly Val Glu Gly Trp Gly Ala Leu Gln Gln
 100 105 110
 His Phe Lys Thr Val Ala Asp Leu Ser Met Val Thr Cys Asn Leu Ser
 115 120 125
 Ser Lys Ile Val Arg Val Val Glu Leu Pro Glu Gly Leu Pro Gln Gly
 130 135 140
 Cys Lys Trp Glu Gln Val Asp Thr Gly Leu Phe Tyr Leu Val Leu Ile
 145 150 155 160
 Leu Pro Ser Cys Leu Thr Leu Leu Val Ala Cys Thr Val Val Phe Leu
 165 170 175
 Thr Phe Lys Lys Pro Leu Leu Gln Val Ile Lys Ser Arg Cys His Trp
 180 185 190
 Ser Ser Ile Tyr
 195

<210> 12

<211> 174

<212> PRT

<213> Mouse

<400> 12

Met Ala Pro Ala Asn Leu Gly Leu Thr Pro His Trp Val Met Leu Leu
 1 5 10 15
 Gly Ala Val Leu Leu Leu Leu Ser Gly Ala Ser Ala Gln Glu Pro
 20 25 30
 Pro Arg Val Gly Cys Ser Glu Tyr Thr Asn Arg Ser Cys Glu Glu Cys
 35 40 45
 Leu Arg Asn Val Ser Cys Leu Trp Cys Asn Glu Asn Lys Ala Cys Met
 50 55 60
 Asp Tyr Pro Val Arg Lys Ile Leu Pro Pro Ala Ser Leu Cys Lys Leu
 65 70 75 80
 Ser Ser Ala Arg Trp Gly Val Cys Trp Val Asn Phe Glu Ala Leu Ile
 85 90 95
 Ile Thr Met Ser Val Leu Gly Gly Ser Val Leu Leu Gly Ile Thr Val
 100 105 110
 Cys Cys Cys Tyr Cys Cys Arg Arg Lys Lys Ser Arg Lys Pro Asp Lys
 115 120 125
 Ser Asp Glu Arg Ala Met Arg Glu Gln Glu Glu Arg Arg Val Arg Gln
 130 135 140
 Glu Glu Arg Arg Ala Glu Met Lys Ser Arg His Asp Glu Ile Arg Lys
 145 150 155 160
 Lys Tyr Gly Leu Phe Lys Glu Gln Asn Pro Tyr Glu Lys Phe
 165 170

<210> 13

<211> 106

<212> PRT

<213> Mouse

<400> 13

Ala Pro Gly Lys Pro Cys Arg Gly Leu Ser His Arg Thr Cys Ile Leu

1	5	10	15
Arg Cys Arg	Pro Met Pro Leu Phe Thr	His Pro Ser Pro	Cys His Leu
	20	25	30
Cys Gly Pro	Cys Ser Thr Thr Ser Pro	Ser Thr Trp Val	Leu Cys Pro
	35	40	45
Leu Pro Met	Ser Pro Leu Cys Pro Thr	Cys Val Ser Thr	Met Thr Leu
	50	55	60
Ala Thr Cys	Thr Cys Pro Trp Ser Thr	Thr Cys Pro Cys	Thr Leu Ala
65	70	75	80
Pro Asn His	Gly Ile Ala Ser Asp Thr	Gln Ser Pro Val	Ser Arg Ala
	85	90	95
Glu Ser Val	Gly Gly Pro Ser Leu	Ile Phe	
	100	105	

<210> 14
 <211> 268
 <212> PRT
 <213> Mouse

<400> 14

Met Ala Leu	Gly Phe Ser Gln Arg Ser	Arg Met Val Ala Ala	Gly Ala
1	5	10	15
Gly Val Thr	Arg Leu Leu Val Leu Leu	Met Val Ala Ala	Ala Pro
	20	25	30
Ser Arg Ala	Arg Gly Ser Gly Cys Arg	Val Gly Ala Ser	Ala Arg Gly
	35	40	45
Thr Gly Ala	Asp Gly Arg Glu Ala Glu	Gly Cys Gly Thr	Val Ala Leu
	50	55	60
Leu Leu Glu	His Ser Phe Glu Leu Gly	Asp Gly Ala Asn	Phe Gln Lys
65	70	75	80
Arg Gly Leu	Leu Leu Trp Asn Gln Gln	Asp Gly Thr Leu	Ser Ala Thr
	85	90	95
Gln Arg Gln	Leu Ser Glu Glu Glu Arg	Gly Arg Leu Arg	Asp Val Ala
	100	105	110
Ala Val Asn	Gly Leu Tyr Arg Val Arg	Val Pro Arg Arg	Pro Gly Thr
	115	120	125
Leu Asp Gly	Ser Glu Ala Gly Gly His	Val Ser Ser Phe	Val Pro Ala
	130	135	140
Cys Ser Leu	Val Glu Ser His Leu Ser	Asp Gln Leu Thr	Leu His Val
145	150	155	160
Asp Val Ala	Gly Asn Val Val Gly Leu	Ser Val Val Val	Tyr Pro Gly
	165	170	175
Gly Cys Arg	Gly Ser Glu Val Glu Asp	Glu Asp Leu Glu	Leu Phe Asn
	180	185	190
Thr Ser Val	Gln Leu Arg Pro Pro Ser	Thr Ala Pro Gly	Pro Glu Thr
	195	200	205
Ala Ala Phe	Ile Glu Arg Leu Glu Met	Glu Gln Ala Gln	Lys Ala Lys
	210	215	220
Asn Pro Gln	Glu Gln Lys Ser Phe Phe	Ala Lys Tyr Trp	Met Tyr Ile
225	230	235	240
Ile Pro Val	Val Leu Phe Leu Met Met	Ser Gly Ala Pro	Asp Ala Gly
	245	250	255
Gly Gln Gly	Gly Gly Gly Gly Gly	Gly Ser Ser Arg	
	260	265	

<210> 15
 <211> 66
 <212> PRT
 <213> Mouse

<400> 15

Met Asp Phe	Leu Val Leu Phe Leu Phe	Tyr Leu Ala Phe	Leu Leu Ile
1	5	10	15
Cys Val Val	Leu Ile Cys Ile Phe Thr	Lys Ser Gln Arg	Leu Lys Ala
	20	25	30
Val Val Leu	Gly Gly Ala Gln Val Ala	Leu Val Leu Gly	Tyr Cys Pro

35 40 45
 Asp Val Asn Thr Val Leu Gly Ala Ser Leu Glu Gly Ser Gln Asp Lys
 50 55 60
 Gly Met
 65

<210> 16
 <211> 338
 <212> PRT
 <213> Mouse

<400> 16
 Met Gly Ala Val Trp Ser Ala Leu Leu Val Gly Gly Gly Leu Ala Gly
 1 5 10 15
 Ala Leu Ile Leu Trp Leu Leu Arg Gly Asp Ser Gly Ala Pro Gly Lys
 20 25 30
 Asp Gly Val Ala Glu Pro Pro Gln Lys Gly Ala Pro Pro Gly Glu Ala
 35 40 45
 Ala Ala Pro Gly Asp Gly Pro Gly Gly Gly Gly Ser Gly Gly Leu Ser
 50 55 60
 Pro Glu Pro Ser Asp Arg Glu Leu Val Ser Lys Ala Glu His Leu Arg
 65 70 75 80
 Glu Ser Asn Gly His Leu Ile Ser Glu Ser Lys Asp Leu Gly Asn Leu
 85 90 95
 Pro Glu Ala Gln Arg Leu Gln Asn Val Gly Ala Asp Trp Val Asn Ala
 100 105 110
 Arg Glu Phe Val Pro Val Gly Lys Ile Pro Asp Thr His Ser Arg Ala
 115 120 125
 Asp Ser Glu Ala Ala Arg Asn Gln Ser Pro Gly Ser His Gly Gly Glu
 130 135 140
 Trp Arg Leu Pro Lys Gly Gln Glu Thr Ala Val Lys Val Ala Gly Ser
 145 150 155 160
 Val Ala Ala Lys Leu Ala Ser Ser Ser Leu Leu Val Asp Arg Ala Lys
 165 170 175
 Ala Val Ser Gln Asp Gln Ala Gly His Glu Asp Trp Glu Val Val Ser
 180 185 190
 Arg His Ser Ser Trp Gly Ser Val Gly Leu Gly Gly Ser Leu Glu Ala
 195 200 205
 Ser Arg Leu Ser Leu Asn Gln Arg Met Asp Asp Ser Thr Asn Ser Leu
 210 215 220
 Val Gly Gly Arg Gly Trp Glu Val Asp Gly Lys Val Ala Ser Leu Lys
 225 230 235 240
 Pro Gln Gln Val Ser Ile Gln Phe Gln Val His Tyr Thr Thr Asn Thr
 245 250 255
 Asp Val Gln Phe Ile Ala Val Thr Gly Asp His Glu Ser Leu Gly Arg
 260 265 270
 Trp Asn Thr Tyr Ile Pro Leu His Tyr Cys Lys Asp Gly Leu Trp Ser
 275 280 285
 His Ser Val Phe Leu Pro Ala Asp Thr Val Val Glu Trp Lys Phe Val
 290 295 300
 Leu Val Glu Asn Lys Glu Val Thr Arg Trp Glu Glu Cys Ser Asn Arg
 305 310 315 320
 Phe Leu Gln Thr Gly His Glu Asp Lys Val Val His Gly Trp Trp Gly
 325 330 335
 Ile His

<210> 17
 <211> 119
 <212> PRT
 <213> Mouse

<400> 17
 Gly Thr Ser Pro Ala Ser Val Leu Arg Ser Val Ser Ser Asp Pro Ser
 1 5 10 15
 Leu Pro Pro Pro Ser Met Ala Ser Leu Leu Cys Cys Gly Pro Lys Leu

<210>	18
<211>	280
<212>	PRT
<213>	Mouse

```
<210> 19
<211> 188
<212> PRT
<213> Mouse
```

<400> 19
Met Ala Leu Cys Ala Arg Ala Ala Leu Leu Leu Gly Val Leu Gln Val
1 5 10 15
Leu Ala Leu Leu Gly Ala Ala Gln Asp Pro Thr Asp Ala Gln Gly Ser

20 25 30
 Ala Ser Gly Asn His Ser Val Leu Thr Ser Asn Ile Asn Ile Thr Glu
 35 40 45
 Asn Thr Asn Gln Thr Met Ser Val Val Ser Asn Gln Thr Ser Glu Met
 50 55 60
 Gln Ser Thr Ala Lys Pro Ser Val Leu Pro Lys Thr Thr Thr Leu Ile
 65 70 75 80
 Thr Val Lys Pro Ala Thr Ile Val Lys Ile Ser Thr Pro Gly Val Leu
 85 90 95
 Pro His Val Thr Pro Thr Ala Ser Lys Ser Thr Pro Asn Ala Ser Ala
 100 105 110
 Ser Pro Asn Ser Thr His Thr Ser Ala Ser Met Thr Thr Pro Ala His
 115 120 125
 Ser Ser Leu Leu Thr Thr Val Thr Val Ser Ala Thr Thr His Pro Thr
 130 135 140
 Lys Gly Lys Gly Ser Lys Phe Asp Ala Gly Ser Phe Val Gly Gly Ile
 145 150 155 160
 Gly Val Asn Thr Gly Ser Phe Ile Tyr Ser Leu His Trp Met Gln Asn
 165 170 175
 Val Leu Phe Lys Lys Arg His Ser Val Pro Lys His
 180 185

<210> 20
 <211> 317
 <212> PRT
 <213> Mouse

<400> 20
 Met Arg Ser Gly Ala Leu Trp Pro Leu Leu Trp Gly Ala Leu Val Trp
 1 5 10 15
 Thr Val Gly Ser Val Gly Ala Val Met Gly Ser Glu Asp Ser Val Pro
 20 25 30
 Gly Gly Val Cys Trp Leu Gln Gln Gly Arg Glu Ala Thr Cys Ser Leu
 35 40 45
 Val Leu Lys Thr Arg Val Ser Arg Glu Glu Cys Cys Ala Ser Gly Asn
 50 55 60
 Ile Asn Thr Ala Trp Ser Asn Phe Thr His Pro Gly Asn Lys Ile Ser
 65 70 75 80
 Leu Leu Gly Phe Leu Gly Leu Val His Cys Leu Pro Cys Lys Asp Ser
 85 90 95
 Cys Asp Gly Val Glu Cys Gly Pro Gly Lys Ala Cys Arg Asn Ala Gly
 100 105 110
 Gly Ala Ser Asn Asn Cys Glu Cys Val Pro Asn Cys Glu Gly Phe Pro
 115 120 125
 Ala Gly Phe Gln Val Cys Gly Ser Asp Gly Ala Thr Tyr Arg Asp Glu
 130 135 140
 Cys Glu Leu Arg Thr Ala Arg Cys Arg Gly His Pro Asp Leu Arg Val
 145 150 155 160
 Met Tyr Arg Gly Arg Cys Gln Lys Ser Cys Ala Gln Val Val Cys Pro
 165 170 175
 Arg Pro Gln Ser Cys Leu Val Asp Gln Thr Gly Ser Ala His Cys Val
 180 185 190
 Val Cys Arg Ala Ala Pro Cys Pro Val Pro Ser Asn Pro Gly Gln Glu
 195 200 205
 Leu Cys Gly Asn Asn Asn Val Thr Tyr Ile Ser Ser Cys His Leu Arg
 210 215 220
 Gln Ala Thr Cys Phe Leu Gly Arg Ser Ile Gly Val Arg His Pro Gly
 225 230 235 240
 Ile Cys Thr Gly Gly Pro Lys Phe Leu Lys Ser Gly Asp Ala Ala Ile
 245 250 255
 Val Asp Met Val Pro Gly Lys Pro Met Cys Val Glu Ser Phe Ser Asp
 260 265 270
 Tyr Pro Pro Leu Gly Arg Phe Ala Val Arg Asp Met Arg Gln Thr Val
 275 280 285
 Ala Val Gly Val Ile Lys Ala Val Asp Lys Lys Ala Ala Gly Ala Gly
 290 295 300

Lys Val Thr Lys Ser Ala Gln Lys Ala Gln Lys Ala Lys
 305 310 315

<210> 21
 <211> 384
 <212> DNA
 <213> Mouse
 <220>
 <221> unsure
 <222> (369)... (369)

<400> 21
 ggtggacttc ggtgggacaa cgtccttcca gtgcaagggtg cgcagtgacg tgaagcctgt
 60
 gatccagtgg ctgaagcggg tggagtacgg ctccgaggga cgccacaact ccaccattga
 120
 tgtgggtggc cagaagtttg tgggtgtgcc cacgggtgat gtgtggtcac ggcctgatgg
 180
 ctctacctc aacaagctgc tcattctctg gggccgccag gatgatgctg gcatgtacat
 240
 ctgcctaggt gcaaatacca tgggtacag tttccgtagc gccttcctca ctgtattacc
 300
 agaccccaaa cctccagggc ctctatggc ttcttcatcg tcattccaaa gcctgccatg
 360
 gcctgtggng atcgcatcc cagc
 384

<210> 22
 <211> 1967
 <212> DNA
 <213> Mouse

<400> 22
 gctgcgcgcc cccgcgctga tccctgtcga gcgtctacgc gcctcgcttc ctttgcttgg
 60
 agctcggcgc cgaggggggc cggaccctgg ctctgcggcc gcgacctggg tcttgcgggc
 120
 ctgagccctg agtggcgtcc agtccagctc ccagtgaccg cggccctgct tcaggtccga
 180
 cgggcgagat gacgcggagc cccgcgctgc tgcgtgctgct attggggggc ctcccgtcgg
 240
 ctgaggcggc gcgaggaccc ccaagaatgg cagacaaagt ggtcccacgg cagggtggccc
 300
 gcctggggcg cactgtgcgg ctacagtgcc cagtggaggg ggaccaccca ccgttgacca
 360
 tgtggaccaa agatggccgc acaatccaca gtggctggag ccgcttccgt gtgctgcccc
 420
 agggctctgaa ggtgaaggag gtggaggccg aggatgccgg tgtttatgtg tgcaaggcca
 480
 ccaatggctt tggcagcctc agcgtcaact acactctcat catcatggat gatattagtc
 540
 cagggaagga gagccctggg ccagggtggtt cttcgggggg ccaggaggac ccagccagcc
 600
 agcagtgggc acggcctcgc ttcacacagc cctccaagat gaggcgccga gtgattgcac
 660
 ggctgtggg tagctctgtg cggctcaagt gtgtggccag tgggcaccca cggccagaca
 720
 tcatgtggat gaaggatgac cagaccttga cgcattctaga ggctagtga cagagaaaga
 780
 agaagtggac actgagcttg aagaacctga agcctgaaga cagtggcaag tacacgtgcc
 840
 gtgtatctaa caaggccggt gccatcaacg ccacctacaa agtggatgta atccagcgga
 900
 ctgcgttcaa gcctgtgctc acaggagac accctgtgaa cacaacgggt gacttcggtg
 960

ggacaacgtc cttccagtgc aaggtgcgca gtgacgtgaa gcctgtgatc cagtggctga
 1020
 agcgggtgga gtacggctcc gagggacgcc acaactccac cattgatgtg ggtggccaga
 1080
 agtttgtggt gttgcccacg ggtgatgtgt ggtcacggcc tgatggctcc tacctcaaca
 1140
 agctgctcat ctctcgggcc cgccaggatg atgctggcat gtacatctgc ctaggtgcaa
 1200
 ataccatggg ctacagtttc cgtagcgctt tcctcactgt attaccagac cccaaacctc
 1260
 cagggcctcc tatggcttct tcctcgtcat ccacaagcct gccatggcct gtggtgatcg
 1320
 gcatcccagc tgggtctgtc ttcattcctag gcactgtgct gctctggctt tgccagacca
 1380
 agaagaagcc atgtgcccc gcatctacac ttctgtgccc tgggcatcgt ccccaggga
 1440
 catcccagga acgcagtggg gacaaggacc tgccctcatt ggctgtgggc atatgtgagg
 1500
 agcatggatc cgccatggcc cccagcaca tcctggcctc tggctcaact gctggcccca
 1560
 agctgtaccc caagctatac acagatgtgc acacacacac acatacacac acctgcactc
 1620
 acacgctctc atgtggaggg caaggttcat caacaccagc atgtccacta tcagtgtctaa
 1680
 atacagcgaa tctccaagca ctgtgtcctg aggtaggcat atgggggcca aggcaacagg
 1740
 ttggggagaat tgagaacaat ggaggaagag tatcttaggg tgccttatgg tggacactca
 1800
 caaacttggc catatagatg tatgtactac cagatgaaca gccagccaga ttcacacacg
 1860
 cacatgttta aacgtgtaaa cgtgtgcaca actgcacaca caacctgaga aaccttcagg
 1920
 aggatttggg gtgtgacttt gcagtgcacat gtagcgatgg ctagttg
 1967

<210> 23
 <211> 1742
 <212> DNA
 <213> Mouse

<400> 23
 gcgcggcgcc cggggccct cgccccgccg cccctcttc cgcacctcgc caagcctcgc
 60
 cgtttatccg cgcgacagc gcgccccgcg cccagcccg gccctagccg ccagcgccca
 120
 ggtagcgccg cccgcccag gccgggcccg ggggcgcggg gggcgggatg cggcgcccgg
 180
 ggcagcgatg accgcgtcgc gctgctcagg ggcccggctc tgaccccggt gctgctgcg
 240
 cgcccccgcg ctgatccctg tcgagcgtct acgcgcctcg cttcctttgc ctggagctcg
 300
 gcgcccaggg gggccggacc ctggctctgc ggccgcgacc tgggtcttgc gggcctgagc
 360
 cctgagtggc gtccagtcca gctcccagt accgcgcccc tgcttcaggt ccgaccggcg
 420
 agatgacgcg gagccccgcg ctgctgctgc tgctattggg ggccctcccg tcggctgagg
 480
 cggcgcgaga tgatattagt ccagggaagg agagccctgg gccagggtgg tcttcggggg
 540
 gccaggagga cccagccagc cagcagtggg cacggcctcg cttcacacag cctccaaga
 600
 tgaggcgccg agtgattgca cggcctgtgg gtagctctgt gcggctcaag tgtgtggcca
 660
 gtgggacccc acggccagac atcatgtgga tgaaggatga ccagacctg acgcatctag
 720
 aggctagtga acacagaaag aagaagtgga cactgagctt gaagaacctg aagcctgaag

780
 acagtggcaa gtacacgtgc cgtgtatcta acaaggccgg tgccatcaac gccacctaca
 840
 aagtggatgt aatccagcgg actcgttcca agcctgtgct cacagggaca caccctgtga
 900
 acacaacggt ggacttcggt gggacaacgt ccttccagtg caaggtgctg agtgacgtga
 960
 agcctgtgat ccagtggctg aagcgggtgg agtacggctc cgagggacgc cacaactcca
 1020
 ccattgatgt gggtagccag aagtttgtgg tgttgccac gggtagtggt tggtcacggc
 1080
 ctgatggctc ctacctcaac aagctgctca tctctcgggc ccgccaggat gatgctggca
 1140
 tgtacatctg cctaggtgca aataccatgg gctacagttt ccgtagcgcc ttctcactg
 1200
 tattaccaga ccccaaacct cctccagggc ctctatggc ttcttcatcg tcatccacaa
 1260
 gcctgccatg gcctgtggtg atcgccatcc cagctggtgc tgtcttcac ctaggcactg
 1320
 tgctgctctg gctttgccag accaagaaga agccatgtgc ccagcatct acacttcctg
 1380
 tgccctggga tcgtccccc gggacatccc gagaacgcag tggtagaca gacctgccct
 1440
 cattggctgt gggcatatgt gaggagcatg gatccgccat ggccccccag cacatcctgg
 1500
 cctctggctc aactgctggc cccaagctgt accccaagct atacacagat gtgcacacac
 1560
 acacacatac acacacctgc actcacacgc tctcatgtgg agggcaaggt tcatcaacac
 1620
 cagcatgtcc actatcagt ctaaatacag cgaatctcca agcactgtgt cctgaggtag
 1680
 gcatatgggg gccaaaggcaa caggttggga gaattgagaa caatggagga agagtatctt
 1740
 ag
 1742

<210> 24
 <211> 1004
 <212> DNA
 <213> Human

<400> 24
 gcggccgcga cccaggtcc ggacaggccg agatgacgcc gagccccctg ttgctgctcc
 60
 tgctgccgcc gctgctgctg ggggccttcc caccggccgc cgccgcccga ggcccccaa
 120
 agatggcgga caaggtggtc ccacggcagg tggccggctg ggccgcactg tggggctgca
 180
 gtgccagtgg agggggaccc gccgcccgtg accatgtgga ccaaggatgg ccgcaccatc
 240
 cacagcggct ggagccgctt ccgcgtgctg ccgcaggggc tgaaggtgaa gcaggtggag
 300
 cgggaggatg ccggcgtgta cgtgtgcaag gccaccaacg gcttcggcag ccttagcgtc
 360
 aactacacc tcgtcgtgct ggatgacatt agcccaggga aggagagcct ggggcccgc
 420
 agctcctctg ggggtcaaga ggaccccgcc agccagcagt gggcacgacc gcgcttcaca
 480
 cagccctcca agatgaggcg ccgggtgatc gcacggcccg tgggtagctc cgtgcccgtc
 540
 aagtgcgtgg ccagcgggca ccctcggccc gacatcacgt ggatgaagga cgaccaggcc
 600
 ttgacgcgcc cagaggccgc tgagcccagg aagaagaagt ggacactgag cctgaagaac
 660
 ctgcggccgg aggacagcgg caaatacacc tgccgcgtgt cgaaccgcgc gggcgccatc
 720

aacgccacct acaaggtgga tgtgatccag cggaccogtt ccaagccogt gctcacaggg
 780
 acgcaccccc tgaacacgac ggtggacttc ggggggacca cgtccttcca gtgcaagggtg
 840
 cgcagcgacg tgaagccggt gatccagtgg ctgaagcgcg tggagtacgg cgccgagggc
 900
 cgccacaact ccaccatcga tgtggggcggc cagaagtttg tgggtctgcc cacgggtgac
 960
 gtgtgggtcg ggcccgacgg ctcctacctc aataagcgcg tccc
 1004

<210> 25
 <211> 478
 <212> DNA
 <213> Mouse

<400> 25
 agaaaaaggc ctcgctaaag caacaaacct gatcattttc aagaaccata ggactgaggt
 60
 gaagccatga agttcttgct gatctcccta gccctatggc tgggcacagt gggcacacgt
 120
 gggacagagc ccgaactcag cgagaccogc cgcaggagcc tacaggtggc tctggaggag
 180
 ttccacaaac acccacctgt gcagttggcc ttccaagaga tcggtgtgga cagagctgaa
 240
 gaagtgtctt tctcagctgg cacctttgtg aggttggat ttaagctcca gcagaccaac
 300
 tgccccaaga aggactggaa aaagccggag tgcacaatca aaccaaaccg ggcggaaatg
 360
 cctggcctgc attaaaatgg accccaaggg taaaattcta ggccggatag tccactgccc
 420
 aattctgaag caagggcctc aggatcctca ggagttgcaa tgcattaaga tagcacag
 478

<210> 26
 <211> 545
 <212> DNA
 <213> Mouse

<400> 26
 agggaaacaac tgccaggag ctgttccagg gaccacacag aaaaaggcct cgctaaagca
 60
 acaaacctga tcattttcaa gaaccatagg actgaggtga agccatgaag ttcttgctga
 120
 tctccctagc cctatggctg ggcacagtgg gcacacgtgg gacagagccc gaactcagcg
 180
 agaccagcg caggagccta caggtggctc tggaggagtt ccacaaacac ccacctgtgc
 240
 agttggcctt ccaagagatc ggtgtggaca gagctgaaga agtgctcttc tcagctggca
 300
 cctttgtgag gttggaattt aagctccagc agaccaactg cccaagaag gactggaaaa
 360
 agccggagtg cacaatcaaa ccaaaccggg gaaggcggaa atgcctggcc tgcattaata
 420
 tggaccccaa gggtaaaatt ctaggccgga tagtccactg cccaattctg aagcaagggc
 480
 ctcaggatcc tcaggagttg caatgcatta agatagcaca ggctggcgaa gacccccacg
 540
 gctac
 545

<210> 27
 <211> 2213
 <212> DNA
 <213> Mouse

<400> 27

gttgcaggcg ctcgagtgca gcatggaaaag tctctgcggg gtcctgggat ttctgctgct
 60
 ggctgcagga ctgcctctcc aggctgcaa gcgatttcgt gatgtgctgg gccatgaaca
 120
 gtatcccaat cacatgagag agcacaacca attacgtggc tgggtcttcgg atgaaaatga
 180
 atgggatgaa cacctgtatc cagtgtggag gaggggagac ggcaggtgga aggactcctg
 240
 ggaaggaggc cgtgtgcagg cagtcctgac cagtgactca ccggctctgg tgggttccaa
 300
 tatcaccttt gtggtgaacc tgggtgtccc cagatgccag aaggaagatg ctaatggcaa
 360
 tatcgtctat gagaagaact gcaggaatga tttgggactg acctctgacc tgcattgcta
 420
 caactggact gcaggggcag atgatggtga ctgggaagat ggcaccagcc gaagccagca
 480
 tctcagggtc ccggacagga ggcccttccc tcgccccat ggatggaaga aatggagctt
 540
 tgtctacgtc ttccacacac ttggccagta tttccaaaaa ctgggtcggt gttcagcacg
 600
 ggtttctata aacacagtca acttgacagc tggccctcag gtcattggaag tgactgtctt
 660
 tcgaagatac ggccgggcat acattcccat ctgaagggtg aaagatgtgt atgtgataac
 720
 agatcagatc cctgtattcg tgacctgtc ccagaagaat gacaggaact tgtctgatga
 780
 gatcttctc agagacctcc ccactgtctt cgatgtcctc attcatgatc ccagccactt
 840
 cctcaacgac tctgccattt cctacaagtg gaactttggg gacaacactg gcctgtttgt
 900
 ctccaacaat cacactttga atcacactta tgtgtcctaat ggaaccttca accttaacct
 960
 caccgtgcaa actgcagtgc ccgggccatg ccctccctc tcgccttcga ctccgcctcc
 1020
 accttcaact ccgcccctac ctccgcccct acctctgccc acattatcaa cacctagccc
 1080
 ctctttaatg cctactggtt acaaatccat ggagctgagt gacatttcca atgaaaactg
 1140
 ccgaataaac agatatggct acttcagagc caccatcaca attgtagagg ggatcctgga
 1200
 agtcagcatc atgcagatag cagatgtccc catgcccaca ccgcagcctg ccaactccct
 1260
 gatggacttc actgtgacct gcaaaggggc ccccccatg gaagcctgta cgatcatctc
 1320
 cgacccacc tgccagatcg ccgagaaccg ggtctgcagc cctgtggctg tggatgggct
 1380
 gtgcctgctg tctgtgagaa gagccttcaa tgggtctggc acctactgtg tgaatttcac
 1440
 tctgggagat gatgcaagcc tggccctcac cagcaccctg atctctatcc ctggcaaaga
 1500
 ccagactcc cctctgagag cagtgaatgg tgcctgatc tccattggct gcctggctgt
 1560
 gcttgtcacc atggttacca tcttctgta caaaaaacac aaggcgtaca agccaatagg
 1620
 aaactgcccc aggaacacgg tcaagggcaa aggcctgagt gttctcctca gccacgcgaa
 1680
 agccccgttc ttccgaggag accaggagaa ggatccattg ctccaggaca agccaaggac
 1740
 actctaagtc tttggccttc cctctgacca ggaaccact cttctgtgca tgtatgtgag
 1800
 ctgtgcagaa gtatgtggct gggaactgtt gttctctaag gattattgta aaatgtatat
 1860
 cgtggcttag ggagtgtgt taaatagcat ttagagaag acatgggaag acttagtgtt
 1920
 tcttcccatc tgtattgtgg tttttacact gttcgtggg tggacacgct gtgtctgaag

1980
 gggaggtggg gtcactgcta cttaaggtcc taggttaact gggggagata ccacagatgc
 2040
 ctcagctttc cacataacat gggcatgaac ccagctaata accacctgaa ggccatgctt
 2100
 catctgcctt ccaactcact gagcatgcct gagctcctga caaaattata atggggcccg
 2160
 gctttgtgta tgggtgcgtgt gtgtacatat tctactcatt aaaaaggtag tct
 2213

<210> 28
 <211> 412
 <212> DNA
 <213> Mouse

<400> 28
 gcgagatccc gcctcgccgc ccctcgagcg cccccagctt ctctgctggc cggaacctgc
 60
 accccgaacc aggaagcacc tggcggcggg cgcgggatgg ctggggccag ctgggggtctc
 120
 cctcggctgg acggtttcat ccttaccgag cgctgggca gtggcacgta cgccacgggtg
 180
 tacaaggcct acgccaagaa ggatactcgg gaagtggtag ccataaaatg cgtggccaag
 240
 aagagtctca acaaggcgtc agtggaaaac ctctgactg agattgagat cctcaagggc
 300
 attcggcacc cccatatcgt gcagctgaaa gacttccagt gggacaatga caatatctac
 360
 ctcatcatgg agttctgtgc agggggtgac ctgtctcgt tcattcatac cc
 412

<210> 29
 <211> 437
 <212> DNA
 <213> Mouse

<400> 29
 cacagtcttg tttctggtgg ctttgatcac tgtggggatg aacactacct atgtagtgct
 60
 ttgccccaaa gaatttgaaa aacctggagc ttgtccaag ccttcaccag aaagtgttgg
 120
 aatttgtgtt gatcaatgct caggagatgg atcctgccct ggcaacatga agtgcgttag
 180
 caatagctgt ggtcatgtct gcaaaactcc tgtcttttaa atggttgaca gccatgtgga
 240
 agatggattc aatcttcata aacatgaatg atggccagcc ccagaagatt tcttctgaat
 300
 tcacagagcc tgtgcttggc tacttcctag ccctagaatt gcattcttgg acaaggaaga
 360
 tctatattgt ggtgacaatg ccctaataatg tctgtgtcca aaataaacta cccttagcat
 420
 tcaaaaaaaaa aaaaaaa
 437

<210> 30
 <211> 126
 <212> PRT
 <213> Mouse

<220>
 <221> UNSURE
 <222> (123)...(123)

<400> 30
 Val Asp Phe Gly Gly Thr Thr Ser Phe Gln Cys Lys Val Arg Ser Asp
 1 5 10 15

Val Lys Pro Val Ile Gln Trp Leu Lys Arg Val Glu Tyr Gly Ser Glu
 20 25 30
 Gly Arg His Asn Ser Thr Ile Asp Val Gly Gly Gln Lys Phe Val Val
 35 40 45
 Leu Pro Thr Gly Asp Val Trp Ser Arg Pro Asp Gly Ser Tyr Leu Asn
 50 55 60
 Lys Leu Leu Ile Ser Arg Ala Arg Gln Asp Asp Ala Gly Met Tyr Ile
 65 70 75 80
 Cys Leu Gly Ala Asn Thr Met Gly Tyr Ser Phe Arg Ser Ala Phe Leu
 85 90 95
 Thr Val Leu Pro Asp Pro Lys Pro Pro Gly Pro Pro Met Ala Ser Ser
 100 105 110
 Ser Ser Ser Thr Ser Leu Pro Trp Pro Val Xaa Gly Ile Pro
 115 120 125

<210> 31
 <211> 529
 <212> PRT
 <213> Mouse

<400> 31
 Met Thr Arg Ser Pro Ala Leu Leu Leu Leu Leu Gly Ala Leu Pro
 1 5 10 15
 Ser Ala Glu Ala Ala Arg Gly Pro Pro Arg Met Ala Asp Lys Val Val
 20 25 30
 Pro Arg Gln Val Ala Arg Leu Gly Arg Thr Val Arg Leu Gln Cys Pro
 35 40 45
 Val Glu Gly Asp Pro Pro Pro Leu Thr Met Trp Thr Lys Asp Gly Arg
 50 55 60
 Thr Ile His Ser Gly Trp Ser Arg Phe Arg Val Leu Pro Gln Gly Leu
 65 70 75 80
 Lys Val Lys Glu Val Glu Ala Glu Asp Ala Gly Val Tyr Val Cys Lys
 85 90 95
 Ala Thr Asn Gly Phe Gly Ser Leu Ser Val Asn Tyr Thr Leu Ile Ile
 100 105 110
 Met Asp Asp Ile Ser Pro Gly Lys Glu Ser Pro Gly Pro Gly Gly Ser
 115 120 125
 Ser Gly Gly Gln Glu Asp Pro Ala Ser Gln Gln Trp Ala Arg Pro Arg
 130 135 140
 Phe Thr Gln Pro Ser Lys Met Arg Arg Arg Val Ile Ala Arg Pro Val
 145 150 155 160
 Gly Ser Ser Val Arg Leu Lys Cys Val Ala Ser Gly His Pro Arg Pro
 165 170 175
 Asp Ile Met Trp Met Lys Asp Asp Gln Thr Leu Thr His Leu Glu Ala
 180 185 190
 Ser Glu His Arg Lys Lys Lys Trp Thr Leu Ser Leu Lys Asn Leu Lys
 195 200 205
 Pro Glu Asp Ser Gly Lys Tyr Thr Cys Arg Val Ser Asn Lys Ala Gly
 210 215 220
 Ala Ile Asn Ala Thr Tyr Lys Val Asp Val Ile Gln Arg Thr Arg Ser
 225 230 235 240
 Lys Pro Val Leu Thr Gly Thr His Pro Val Asn Thr Thr Val Asp Phe
 245 250 255
 Gly Gly Thr Thr Ser Phe Gln Cys Lys Val Arg Ser Asp Val Lys Pro
 260 265 270
 Val Ile Gln Trp Leu Lys Arg Val Glu Tyr Gly Ser Glu Gly Arg His
 275 280 285
 Asn Ser Thr Ile Asp Val Gly Gly Gln Lys Phe Val Val Leu Pro Thr
 290 295 300
 Gly Asp Val Trp Ser Arg Pro Asp Gly Ser Tyr Leu Asn Lys Leu Leu
 305 310 315 320
 Ile Ser Arg Ala Arg Gln Asp Asp Ala Gly Met Tyr Ile Cys Leu Gly
 325 330 335
 Ala Asn Thr Met Gly Tyr Ser Phe Arg Ser Ala Phe Leu Thr Val Leu
 340 345 350
 Pro Asp Pro Lys Pro Pro Gly Pro Pro Met Ala Ser Ser Ser Ser

```

      355      360      365
Thr Ser Leu Pro Trp Pro Val Ile Gly Ile Pro Ala Gly Ala Val
 370      375      380
Phe Ile Leu Gly Thr Val Leu Leu Trp Leu Cys Gln Thr Lys Lys Lys
385      390      395      400
Pro Cys Ala Pro Ala Ser Thr Leu Pro Val Pro Gly His Arg Pro Pro
      405      410      415
Gly Thr Ser Arg Glu Arg Ser Gly Asp Lys Asp Leu Pro Ser Leu Ala
      420      425      430
Val Gly Ile Cys Glu Glu His Gly Ser Ala Met Ala Pro Gln His Ile
      435      440      445
Leu Ala Ser Gly Ser Thr Ala Gly Pro Lys Leu Tyr Pro Lys Leu Tyr
      450      455      460
Thr Asp Val His Thr His Thr His Thr His Thr Cys Thr His Thr Leu
465      470      475      480
Ser Cys Gly Gly Gln Gly Ser Ser Thr Pro Ala Cys Pro Leu Ser Val
      485      490      495
Leu Asn Thr Ala Asn Leu Gln Ala Leu Cys Pro Glu Val Gly Ile Trp
      500      505      510
Gly Pro Arg Gln Gln Val Gly Arg Ile Glu Asn Asn Gly Gly Arg Val
      515      520      525
Ser

```

```

<210> 32
<211> 439
<212> PRT
<213> Mouse

```

```

      <400> 32
Met Thr Arg Ser Pro Ala Leu Leu Leu Leu Leu Gly Ala Leu Pro
 1      5      10      15
Ser Ala Glu Ala Ala Arg Asp Asp Ile Ser Pro Gly Lys Glu Ser Pro
      20      25      30
Gly Pro Gly Gly Ser Ser Gly Gly Gln Glu Asp Pro Ala Ser Gln Gln
      35      40      45
Trp Ala Arg Pro Arg Phe Thr Gln Pro Ser Lys Met Arg Arg Arg Val
      50      55      60
Ile Ala Arg Pro Val Gly Ser Ser Val Arg Leu Lys Cys Val Ala Ser
65      70      75      80
Gly His Pro Arg Pro Asp Ile Met Trp Met Lys Asp Asp Gln Thr Leu
      85      90      95
Thr His Leu Glu Ala Ser Glu His Arg Lys Lys Lys Trp Thr Leu Ser
      100      105      110
Leu Lys Asn Leu Lys Pro Glu Asp Ser Gly Lys Tyr Thr Cys Arg Val
      115      120      125
Ser Asn Lys Ala Gly Ala Ile Asn Ala Thr Tyr Lys Val Asp Val Ile
      130      135      140
Gln Arg Thr Arg Ser Lys Pro Val Leu Thr Gly Thr His Pro Val Asn
145      150      155      160
Thr Thr Val Asp Phe Gly Gly Thr Thr Ser Phe Gln Cys Lys Val Arg
      165      170      175
Ser Asp Val Lys Pro Val Ile Gln Trp Leu Lys Arg Val Glu Tyr Gly
      180      185      190
Ser Glu Gly Arg His Asn Ser Thr Ile Asp Val Gly Gly Gln Lys Phe
      195      200      205
Val Val Leu Pro Thr Gly Asp Val Trp Ser Arg Pro Asp Gly Ser Tyr
      210      215      220
Leu Asn Lys Leu Leu Ile Ser Arg Ala Arg Gln Asp Asp Ala Gly Met
225      230      235      240
Tyr Ile Cys Leu Gly Ala Asn Thr Met Gly Tyr Ser Phe Arg Ser Ala
      245      250      255
Phe Leu Thr Val Leu Pro Asp Pro Lys Pro Pro Pro Gly Pro Pro Met
      260      265      270
Ala Ser Ser Ser Ser Ser Thr Ser Leu Pro Trp Pro Val Val Ile Gly
      275      280      285

```

Ile Pro Ala Gly Ala Val Phe Ile Leu Gly Thr Val Leu Leu Trp Leu
 290 295 300
 Cys Gln Thr Lys Lys Lys Pro Cys Ala Pro Ala Ser Thr Leu Pro Val
 305 310 315 320
 Pro Gly His Arg Pro Pro Gly Thr Ser Arg Glu Arg Ser Gly Asp Lys
 325 330 335
 Asp Leu Pro Ser Leu Ala Val Gly Ile Cys Glu Glu His Gly Ser Ala
 340 345 350
 Met Ala Pro Gln His Ile Leu Ala Ser Gly Ser Thr Ala Gly Pro Lys
 355 360 365
 Leu Tyr Pro Lys Leu Tyr Thr Asp Val His Thr His Thr His Thr His
 370 375 380
 Thr Cys Thr His Thr Leu Ser Cys Gly Gly Gln Gly Ser Ser Thr Pro
 385 390 395 400
 Ala Cys Pro Leu Ser Val Leu Asn Thr Ala Asn Leu Gln Ala Leu Cys
 405 410 415
 Pro Glu Val Gly Ile Trp Gly Pro Arg Gln Gln Val Gly Arg Ile Glu
 420 425 430
 Asn Asn Gly Gly Arg Val Ser
 435

<210> 33
 <211> 322
 <212> PRT
 <213> Human

<400> 33

Arg Arg Ala Pro Cys Cys Cys Ser Cys Cys Arg Arg Cys Cys Trp Gly
 1 5 10 15
 Pro Ser His Arg Pro Pro Pro Pro Glu Ala Pro Gln Arg Trp Arg Thr
 20 25 30
 Arg Trp Ser His Gly Arg Trp Pro Ala Gly Pro His Cys Ala Ala Ala
 35 40 45
 Val Pro Val Glu Gly Asp Pro Pro Leu Thr Met Trp Thr Lys Asp
 50 55 60
 Gly Arg Thr Ile His Ser Gly Trp Ser Arg Phe Arg Val Leu Pro Gln
 65 70 75 80
 Gly Leu Lys Val Lys Gln Val Glu Arg Glu Asp Ala Gly Val Tyr Val
 85 90 95
 Cys Lys Ala Thr Asn Gly Phe Gly Ser Leu Ser Val Asn Tyr Thr Leu
 100 105 110
 Val Val Leu Asp Asp Ile Ser Pro Gly Lys Glu Ser Leu Gly Pro Asp
 115 120 125
 Ser Ser Ser Gly Gly Gln Glu Asp Pro Ala Ser Gln Gln Trp Ala Arg
 130 135 140
 Pro Arg Phe Thr Gln Pro Ser Lys Met Arg Arg Arg Val Ile Ala Arg
 145 150 155 160
 Pro Val Gly Ser Ser Val Arg Leu Lys Cys Val Ala Ser Gly His Pro
 165 170 175
 Arg Pro Asp Ile Thr Trp Met Lys Asp Asp Gln Ala Leu Thr Arg Pro
 180 185 190
 Glu Ala Ala Glu Pro Arg Lys Lys Lys Trp Thr Leu Ser Leu Lys Asn
 195 200 205
 Leu Arg Pro Glu Asp Ser Gly Lys Tyr Thr Cys Arg Val Ser Asn Arg
 210 215 220
 Ala Gly Ala Ile Asn Ala Thr Tyr Lys Val Asp Val Ile Gln Arg Thr
 225 230 235 240
 Arg Ser Lys Pro Val Leu Thr Gly Thr His Pro Val Asn Thr Thr Val
 245 250 255
 Asp Phe Gly Gly Thr Thr Ser Phe Gln Cys Lys Val Arg Ser Asp Val
 260 265 270
 Lys Pro Val Ile Gln Trp Leu Lys Arg Val Glu Tyr Gly Ala Glu Gly
 275 280 285
 Arg His Asn Ser Thr Ile Asp Val Gly Gly Gln Lys Phe Val Val Leu
 290 295 300
 Pro Thr Gly Asp Val Trp Ser Arg Pro Asp Gly Ser Tyr Leu Asn Lys

305
Pro Leu

310

315

320

<210> 34
<211> 102
<212> PRT
<213> Mouse

<400> 34

Met	Lys	Phe	Leu	Leu	Ile	Ser	Leu	Ala	Leu	Trp	Leu	Gly	Thr	Val	Gly
1			5						10					15	
Thr	Arg	Gly	Thr	Glu	Pro	Glu	Leu	Ser	Glu	Thr	Gln	Arg	Arg	Ser	Leu
			20					25					30		
Gln	Val	Ala	Leu	Glu	Glu	Phe	His	Lys	His	Pro	Pro	Val	Gln	Leu	Ala
		35				40						45			
Phe	Gln	Glu	Ile	Gly	Val	Asp	Arg	Ala	Glu	Glu	Val	Leu	Phe	Ser	Ala
	50					55					60				
Gly	Thr	Phe	Val	Arg	Leu	Glu	Phe	Lys	Leu	Gln	Gln	Thr	Asn	Cys	Pro
65					70					75				80	
Lys	Lys	Asp	Trp	Lys	Lys	Pro	Glu	Cys	Thr	Ile	Lys	Pro	Asn	Gly	Ala
			85						90					95	
Glu	Met	Pro	Gly	Leu	His										
			100												

<210> 35
<211> 147
<212> PRT
<213> Mouse

<400> 35

Met	Lys	Phe	Leu	Leu	Ile	Ser	Leu	Ala	Leu	Trp	Leu	Gly	Thr	Val	Gly
1			5						10					15	
Thr	Arg	Gly	Thr	Glu	Pro	Glu	Leu	Ser	Glu	Thr	Gln	Arg	Arg	Ser	Leu
			20					25					30		
Gln	Val	Ala	Leu	Glu	Glu	Phe	His	Lys	His	Pro	Pro	Val	Gln	Leu	Ala
		35				40						45			
Phe	Gln	Glu	Ile	Gly	Val	Asp	Arg	Ala	Glu	Glu	Val	Leu	Phe	Ser	Ala
	50					55					60				
Gly	Thr	Phe	Val	Arg	Leu	Glu	Phe	Lys	Leu	Gln	Gln	Thr	Asn	Cys	Pro
65					70					75				80	
Lys	Lys	Asp	Trp	Lys	Lys	Pro	Glu	Cys	Thr	Ile	Lys	Pro	Asn	Gly	Arg
			85						90					95	
Arg	Arg	Lys	Cys	Leu	Ala	Cys	Ile	Lys	Met	Asp	Pro	Lys	Gly	Lys	Ile
			100					105					110		
Leu	Gly	Arg	Ile	Val	His	Cys	Pro	Ile	Leu	Lys	Gln	Gly	Pro	Gln	Asp
		115				120						125			
Pro	Gln	Glu	Leu	Gln	Cys	Ile	Lys	Ile	Ala	Gln	Ala	Gly	Glu	Asp	Pro
	130					135						140			
His	Gly	Tyr													
145															

<210> 36
<211> 574
<212> PRT
<213> Mouse

<400> 36

Met	Glu	Ser	Leu	Cys	Gly	Val	Leu	Gly	Phe	Leu	Leu	Leu	Ala	Ala	Gly
1			5						10					15	
Leu	Pro	Leu	Gln	Ala	Ala	Lys	Arg	Phe	Arg	Asp	Val	Leu	Gly	His	Glu
			20					25					30		
Gln	Tyr	Pro	Asn	His	Met	Arg	Glu	His	Asn	Gln	Leu	Arg	Gly	Trp	Ser
		35				40						45			
Ser	Asp	Glu	Asn	Glu	Trp	Asp	Glu	His	Leu	Tyr	Pro	Val	Trp	Arg	Arg
	50					55					60				

Gly Asp Gly Arg Trp Lys Asp Ser Trp Glu Gly Gly Arg Val Gln Ala
 65 70 75 80
 Val Leu Thr Ser Asp Ser Pro Ala Leu Val Gly Ser Asn Ile Thr Phe
 85 90 95
 Val Val Asn Leu Val Phe Pro Arg Cys Gln Lys Glu Asp Ala Asn Gly
 100 105 110
 Asn Ile Val Tyr Glu Lys Asn Cys Arg Asn Asp Leu Gly Leu Thr Ser
 115 120 125
 Asp Leu His Val Tyr Asn Trp Thr Ala Gly Ala Asp Asp Gly Asp Trp
 130 135 140
 Glu Asp Gly Thr Ser Arg Ser Gln His Leu Arg Phe Pro Asp Arg Arg
 145 150 155 160
 Pro Phe Pro Arg Pro His Gly Trp Lys Lys Trp Ser Phe Val Tyr Val
 165 170 175
 Phe His Thr Leu Gly Gln Tyr Phe Gln Lys Leu Gly Arg Cys Ser Ala
 180 185 190
 Arg Val Ser Ile Asn Thr Val Asn Leu Thr Ala Gly Pro Gln Val Met
 195 200 205
 Glu Val Thr Val Phe Arg Arg Tyr Gly Arg Ala Tyr Ile Pro Ile Ser
 210 215 220
 Lys Val Lys Asp Val Tyr Val Ile Thr Asp Gln Ile Pro Val Phe Val
 225 230 235 240
 Thr Met Ser Gln Lys Asn Asp Arg Asn Leu Ser Asp Glu Ile Phe Leu
 245 250 255
 Arg Asp Leu Pro Ile Val Phe Asp Val Leu Ile His Asp Pro Ser His
 260 265 270
 Phe Leu Asn Asp Ser Ala Ile Ser Tyr Lys Trp Asn Phe Gly Asp Asn
 275 280 285
 Thr Gly Leu Phe Val Ser Asn Asn His Thr Leu Asn His Thr Tyr Val
 290 295 300
 Leu Asn Gly Thr Phe Asn Leu Asn Leu Thr Val Gln Thr Ala Val Pro
 305 310 315 320
 Gly Pro Cys Pro Pro Ser Pro Ser Thr Pro Pro Pro Pro Ser Thr
 325 330 335
 Pro Pro Ser Pro Pro Pro Ser Pro Leu Pro Thr Leu Ser Thr Pro Ser
 340 345 350
 Pro Ser Leu Met Pro Thr Gly Tyr Lys Ser Met Glu Leu Ser Asp Ile
 355 360 365
 Ser Asn Glu Asn Cys Arg Ile Asn Arg Tyr Gly Tyr Phe Arg Ala Thr
 370 375 380
 Ile Thr Ile Val Glu Gly Ile Leu Glu Val Ser Ile Met Gln Ile Ala
 385 390 395 400
 Asp Val Pro Met Pro Thr Pro Gln Pro Ala Asn Ser Leu Met Asp Phe
 405 410 415
 Thr Val Thr Cys Lys Gly Ala Thr Pro Met Glu Ala Cys Thr Ile Ile
 420 425 430
 Ser Asp Pro Thr Cys Gln Ile Ala Gln Asn Arg Val Cys Ser Pro Val
 435 440 445
 Ala Val Asp Gly Leu Cys Leu Leu Ser Val Arg Arg Ala Phe Asn Gly
 450 455 460
 Ser Gly Thr Tyr Cys Val Asn Phe Thr Leu Gly Asp Asp Ala Ser Leu
 465 470 475 480
 Ala Leu Thr Ser Thr Leu Ile Ser Ile Pro Gly Lys Asp Pro Asp Ser
 485 490 495
 Pro Leu Arg Ala Val Asn Gly Val Leu Ile Ser Ile Gly Cys Leu Ala
 500 505 510
 Val Leu Val Thr Met Val Thr Ile Leu Leu Tyr Lys Lys His Lys Ala
 515 520 525
 Tyr Lys Pro Ile Gly Asn Cys Pro Arg Asn Thr Val Lys Gly Lys Gly
 530 535 540
 Leu Ser Val Leu Leu Ser His Ala Lys Ala Pro Phe Phe Arg Gly Asp
 545 550 555 560
 Gln Glu Lys Asp Pro Leu Leu Gln Asp Lys Pro Arg Thr Leu
 565 570

<210> 37

<211> 137
 <212> PRT
 <213> Mouse

<400> 37

```

Ala Glu Ser Arg Leu Ala Ala Pro Arg Ala Pro Pro Ala Ser Leu Leu
 1           5           10           15
Ala Gly Thr Cys Thr Pro Asn Gln Glu Ala Pro Gly Gly Gly Arg Gly
 20           25           30
Met Ala Gly Pro Ser Trp Gly Leu Pro Arg Leu Asp Gly Phe Ile Leu
 35           40           45
Thr Glu Arg Leu Gly Ser Gly Thr Tyr Ala Thr Val Tyr Lys Ala Tyr
 50           55           60
Ala Lys Lys Asp Thr Arg Glu Val Val Ala Ile Lys Cys Val Ala Lys
 65           70           75           80
Lys Ser Leu Asn Lys Ala Ser Val Glu Asn Leu Leu Thr Glu Ile Glu
 85           90           95
Ile Leu Lys Gly Ile Arg His Pro His Ile Val Gln Leu Lys Asp Phe
100           105           110
Gln Trp Asp Asn Asp Asn Ile Tyr Leu Ile Met Glu Phe Cys Ala Gly
115           120           125
Gly Asp Leu Ser Arg Phe Ile His Thr
130           135

```

<210> 38
 <211> 72
 <212> PRT
 <213> Mouse

<400> 38

```

Thr Val Leu Phe Leu Val Ala Leu Ile Thr Val Gly Met Asn Thr Thr
 1           5           10           15
Tyr Val Val Ser Cys Pro Lys Glu Phe Glu Lys Pro Gly Ala Cys Pro
 20           25           30
Lys Pro Ser Pro Glu Ser Val Gly Ile Cys Val Asp Gln Cys Ser Gly
 35           40           45
Asp Gly Ser Cys Pro Gly Asn Met Lys Cys Cys Ser Asn Ser Cys Gly
 50           55           60
His Val Cys Lys Thr Pro Val Phe
 65           70

```

<210> 39
 <211> 1587
 <212> DNA
 <213> Mouse

<400> 39

```

gcggcgcggg tagagggcgg tgggcggcga gcggcgatgg gccgcgcctg gggcttgctc
60
gttggaactcc tgggcgctgt gtggctgctg cgcttgggcc acggcgagga gcggcgcccg
120
gagacagcgg cacagcgtg cttctgccag gttagtgggtt acctggacga ctgtacctgt
180
gatgtcgaga ccatacataa gttaataaac tacagacttt tccaagact acaaaagctt
240
cttgaaagtg actactttag atattacaag gtgaacttga agaagccttg tcctttctgg
300
aatgacatca accagtgtgg aagaagagac tgtgccgtca aacctgcca ttctgatgaa
360
gttcctgatg gaattaagtc tgcgagctac aagtattctg aggaagccaa ccgcattgaa
420
gaatgtgagc aagctgagcg acttgagacc gtggatgagt ctctgagtga ggagaccag
480
aaagctgtac ttcagtggac caagcatgat gattcgtcag acagcttctg cgaaattgac
540
gatatacagt ccccgatgc tgagtatgtg gacttactcc ttaacctga gcgctacaca

```

600
 ggctacaagg ggccagacgc ttggaggata tggagtgtca tctatgaaga aaactgtttt
 660
 aagccacaga caattcaaag gcctttggct tctgggagag gaaaaagtaa agagaacaca
 720
 ttttacaact ggctagaagg cctctgtgta gaaaagagag cattctacag acttatatct
 780
 ggctgcacg caagcattaa tgtgcatttg agtgcaagg atcttttaca agatacttgg
 840
 ctggaaaaga aatgggggtca caatgtcaca gagttccagc agcgctttga tgggattctg
 900
 actgaaggag aaggccacg aaggctgagg aacttgtact tctgtacct gatagagtta
 960
 agggctctct ccaaagtgt tccatttttt gagcgccag attttcagct cttcactggg
 1020
 aataaagttc aggatgcaga aaacaaagcg ttacttctgg agatacttca tgaaatcaag
 1080
 tcatttcctt tgcacttcga tgagaattct ttttttgctg gggataaaaa cgaagcacat
 1140
 aaactaaagg aggacttccg gctacacttt aggaacattt caagaatcat ggactgtgtt
 1200
 ggctgcttca agtgccgct gtggggcaag cttcagacgc aggggctggg cactgctctg
 1260
 aagatcttgt tttccgaaaa actgatcgca aatatgccg aaagcggacc aagttatgag
 1320
 ttccagctaa ccagacaaga aatagtatca ctgtttaatg catttggaag gatttccaca
 1380
 agtgtgagag aactagagaa cttcaggcac ttgttacaga atgttactg aggaggacgg
 1440
 ttggaatgtg cctgtttctg cacaggggaa ttgaagggc aaaatctctt ttgccccat
 1500
 ggttgcaatg tactgtccta agcccaacgt ttatataaac ctgcttttgt taaagaaaaa
 1560
 aaaaaaaaaa aaaaaaaaaa aaaaaaa
 1587

<210> 40
 <211> 2435
 <212> DNA
 <213> Mouse

<400> 40
 ggaggaggct cggcgccccc ctccctggccc cctccccccc ggtgctggct ccatgtctgt
 60
 gtgaccggcc gcaggggtag gattcaggcc cgacgcgggg cgggcgggag acggcgggctg
 120
 aggtgagagg cggcggcggc ggcgcggctc gggcaccggc ccccagcgg gaggatgaag
 180
 cggcggaaac ccgactgcag taagctccgc cgccccctga agcggaaacc gatcaccgag
 240
 ggtatctacg gcagtacatt tttatacctg aaattcctgg tagtgtgggc acttgtcctc
 300
 cttgccgact ttgtcctgga gttccgattt gaatacctgt ggccgttctg gcttttcac
 360
 agaagcgtct atgattcctt cagataccaa ggactggcct tctcagtatt tttgtttgt
 420
 gtagcattca cttcaaata catatgtctc ctcttcattc ccatacaatg gcttttttct
 480
 gctgctagca catatgtatg ggtccagtac gtatggcaca cagaaagggg agtgtgtttg
 540
 cctacagtgt cactctggat cctctttgtt tatattgaag cagcaattag atttaaagat
 600
 ctgaaaaact ttcattgtag cctttgtcga ccgtttgctg ctcactgcat tggataccct
 660
 gtggtgactt tgggctttgg cttcaaaagt tatgtgagct acaaaatgcg gtttaaggag
 720

cagaaggaag ttcagaagga gaacgagttt tacatgcagc ttcttcagca ggccctccct
 780
 ccagagcagc aaatgttgca gaagcaggag aaggaggctg aggaagcagc caagggattg
 840
 ccggacatgg attcctcgat ccttatacac cacaacggag gcatcccagc caacaaaaaa
 900
 ctgtccacaa cgttgccaga gatagaatat cgagaaaaag ggaaagagaa ggacaaggat
 960
 gccaaagaaac acaaccttgg aataaataac aacaacattc tacaacctgt agactctaag
 1020
 atacaagaga ttgagtatat ggaaaacat atcaatagta aaagattaaa caatgatctt
 1080
 gtgggaagta cagaaaatct cttaaaagag gactcatgca ctgcttcctc aaaaaattac
 1140
 aaaaatgcc a gtggagttgt gaactcctcg cctcgaagtc acagcgctac aaatggaagc
 1200
 attccttcct cgtctagtaa aaacgagaag aagcagaagt gcaccagcaa gggcccgagt
 1260
 gcacacaagg acttaatgga gaactgtatt cctaacaacc agctgagcaa accagacgcg
 1320
 ctggtaaggc tggaacaaga cattaaaaag ctaaaggctg acctgcaagc cagccggcaa
 1380
 gtggagcaag agctgcgcag tcagatcagc gccctctcaa gcacagagcg aggcattccg
 1440
 tcagaaatgg gccagctccg gcaggagaac gagctgctgc agaacaagtt acacaatgcc
 1500
 gtgcaaatga agcaaaaaga caagcagaat atcagccagc tagagaagaa gctaaaggct
 1560
 gagcaggaag cccgaagctt tgtagaaaag cagctaattg aggagaaaaa aaggagaag
 1620
 ttagaagaag ccacagctgc acgggctggt gcccttgctg ctgcatctag gggagagtgc
 1680
 acggaaacct tacggagtgc gatcagagag ctagaagctg agggcaagaa gctcacaatg
 1740
 gacatgaaag tgaaggagga gcagatcagg gaactggaac tgaaggttca ggagcttcg
 1800
 aagtacaaag aaaacgagaa ggacaccgag gtattgatgt cagccctctc cgccatgcaa
 1860
 gacaaaacgc aacacctaga gaacagtctc agcgagagaa cgaggatcaa gctggacctc
 1920
 ttctctgcac ttggtgatgc aaagcggcag ctggagattg cccaggggca aattcttcag
 1980
 aaagaccagg aaatcaagga cctaaaacag aaaatagctg aagtcattggc tgcattgccc
 2040
 agcataacat acagtgtctg caccagtccc ctgagccccg tgtccccca ctactcttc
 2100
 aagtttgtgg agaccagccc ctctggactt gaccctaag cctctgtcta ccagcccttg
 2160
 aagaagtga ggccaactgt gtgctcgccc aacatttgca accaggaggc ttcgaaaagc
 2220
 agcgtctctg gcagtcaaga taataaagtt gatatttgtt tttgtgggac tgtatatgtt
 2280
 gtcattttta aaggggggaa ataacatcca agtctgatta gaaccgcca tcagttgttc
 2340
 ttggaagttt ttagaagacc tcacggactt tgcagtttat tttgtttggc caacacatta
 2400
 aaccattct tggatttcaa gtaaaaaaaa aaaaa
 2435

<210> 41
 <211> 1720
 <212> DNA
 <213> Mouse

<400> 41
 gtgacgcga ggcccaggcg gaagtgcggg cggaggatcc cgagccggat cccgagccgg

60
 gcgcggggct cggggctcgc aggagcggct ggctcccgcg atggcgagcc tatggtgcgg
 120
 aaacctgctg cggtctgggt cggggctcaa catgtcctgc ctggcgctgt cggtgctgct
 180
 gctcgcgcag ctgacaggcg ccgccaagaa ttttgaagat gtgagatgta aatgcatctg
 240
 ccctccctat aaagagaatc ctgggcacat ttataataag aatatatctc agaaagattg
 300
 tgattgcctt catgtcgtgg agcccatgcc tgtacgggga cctgatgtag aagcatactg
 360
 tctacgctgt gaatgcaaat acgaagagag aagctctgtc acaatcaagg ttaccattat
 420
 aatttatctc tctattttgg gccttctgct tctgtacatg gtatatctta ccttagttga
 480
 gcccatcctg aagaggcgcc tctttggaca ctcccagctg ttgcagagcg atgatgacgt
 540
 tggggatcac cagccttttg caaatgccca tgatgtgctg gcccgctctc gcagccgagc
 600
 caatgttcta aacaagggtg agtacgctca gcagcgctgg aagctccagg tccaggagca
 660
 gcgaaagtct gtcttcgacc gacacgttgt cctcagctaa ctgggaactg gaatcagggtg
 720
 actaggaaga acacgcagac aactgggaag aattgtctgg gtgtccgtgc gttttaatgc
 780
 catgtttgtt tttaaaaatc cttgctggat ggaggaagac tccaaactgg aagcaaaccc
 840
 catgcttggg attttcctgt taatatatta atagagacat ttttacagca cacagttcca
 900
 agtcaaccag taagtctttt cctacttgtg acttttacta ataaaattaa gctgcctgtg
 960
 agttatcttg aagccccgtg cctggaacaa gctctctctt tcttgccaca cagttctaac
 1020
 ttggtgttca agataacttc cagggtgtgtt tttgcttctc tttcttgggtg tgggagagag
 1080
 aggggaaggat gccttgggag tgcttgagta gcttctcaag tgtcttttcc agacagactt
 1140
 atgaatactt cagaccctct acttcacact tgtaaatgct ccagtgtagc tggcttgtca
 1200
 gcgtgctggc ctccccactt gacttttgca ctgactacat tacctaagat tctgggttagc
 1260
 ctgtggctgc atttcatgac cagttggatc tgaaatgcct gggggctcct cacaaaatga
 1320
 agatttgtt catgcactgt gatgtctgac gcaacatgtt ctagaacaga ctggccatct
 1380
 gctagtttac actgatacct aaacacagtc tcagtgtgtg tggcttctct catcttcttc
 1440
 tagtagctct aaggacttga acatttagaa taaagacatt ttctcttaag cccaagcctc
 1500
 cctggatgat tgacgtacaa atactgatca gccttttctg tcttgctgag aggcagttct
 1560
 ttgaactgat gtgggcagct ttgaacaagg actagagttc agattgcctc tctctgagaa
 1620
 gtctaacagt tattggataa ctggcttttt tcttcttaca tctcttttgg aatgtaacaa
 1680
 taaaataatt tacaaaaccc aaaaaaaaaa aaaaaaaaaa
 1720

<210> 42
 <211> 1008
 <212> DNA
 <213> Mouse

<400> 42
 gggaaaagca agatcttgca caaggtcccc tccggctggc tgctggcaaa ggaaagggtgc
 60

catgggacct ctccaccagt ttctcctgct gctgatcaca gccctgtccc aagccctcaa
 120
 caccacgggtg ctgcagggca tggccggcca gtccctgagg gtgtcatgta cttatgacgc
 180
 cttgaagcac tgggggagac gcaaggcctg gtgtcggcag ctgggtgagg agggcccatg
 240
 ccagcgtgtg gtgagcacac acggtgtgtg gctgctggcc ttcctgaaga agcggaatgg
 300
 gagcacagtc atcgcatatg acacccttgc tggaaaccgtc accatcactc tgaagaacct
 360
 ccaagccgggt gacgcggggc tctaccagtg tcagagtctc cgaggccgag aggctgaggt
 420
 cctgcagaaa gtactgggtg aggtgctgga ggaccctcta gatgaccaag atgctggaga
 480
 tctctgggtc cccgaggagt catcgagttt cgagggtgcc caagtggaac acagcacctc
 540
 caggaatcaa gagacctcct tcccacccac ctccattctt ctctcctggt cctgcgttct
 600
 cctgagcaag tttcttgtag ccagcatcct ctgggtgtgt gccaggggca ggcagaagcc
 660
 gggaacacct gtggtcagag ggctggactg tggccaagat gctgggcacc aacttcagat
 720
 cctcactgga cccggaggta cgtgagagaa ttctgagtgg gaggagaact acagcttaag
 780
 tccagccagg agtcaatcca gctgcatgc tctccctcc tccaccaaga cttctgttct
 840
 tgctactttt gcttcagagg ccgcctctgc ctcaagccca cctatcctgg gagcaggaat
 900
 actgggtgtg acatctgtgt tgagtgggga agacagctgg atgggtgtct gtcaagttct
 960
 gcacttttga cattaacat tctccacaca ccaaaaaaaaa aaaaaaaaa
 1008

<210> 43
 <211> 1871
 <212> DNA
 <213> Mouse

<400> 43
 ggcagcggca gtgtagagcc gggccgggag gccgatcctg cgggtctgga gtccggcggg
 60
 accatgggga ccggggctgg tgggcccagt gtccctggcg tgctgttcgc cgtgtgtgct
 120
 ccgctccggt tgcaggcgga ggagctgggt gatggctgtg ggcacatagt gacctctcag
 180
 gacagtggca caatgacatc taagaattat ccagggaactt accccaatta cactgtgtgt
 240
 gaaaagatca tcacagtccc aaagggaag agacttatc tgagggtggg agatttgaac
 300
 attgagtcca agacctgcgc ttctgactat ctctcttca gcagtgaac agatcagtat
 360
 ggtccatatt gtgggagttg ggctgttccc aaagaactcc ggctgaactc aaacgaagtg
 420
 actgtcctct tcaagagtgg atctcacatt tctggccggg gctttctgct gacctacgc
 480
 agcagtgaac atccagattt aataacctgt ttggaacgag gcagccatta ttctgaggaa
 540
 aaatacagca aattctgccc agctggctgt agagacatag cagagatat ttctgggaat
 600
 acaaaagatg gttacagaga tacctcttta ttgtgcaaag ctgccatcca cgcagggatc
 660
 atcacagatg aactaggtgg ccacatcaac ttgcttcaga gcaaaggat aagtcactat
 720
 gaaggactcc tggccaatgg cgtgctctcc cggcatggtt ctttgtcgga aaagcgattt
 780
 ctttttaciaa cccaggaat gaatattaca actgtggcga ttccatcagt gatcttcac

840
 gccctccttc tgactggaat ggggatcttt gcaatctgta gaaagaggaa aaagaaagga
 900
 aatccatatg tgtcagctga cgctcagaaa acaggctgtt ggaagcagat taaatatccc
 960
 ttgtccaggc atcagtcgac ggaatttacc atcagctatg acaatgaaaa agagatgaca
 1020
 caaaagttag atctcatcac tagtgatatg gcagattatc agcagcctct catgattggc
 1080
 acaggcacag tcgcgagaaa gggctctacc ttccgacca tggacacaga cactgaggag
 1140
 gtcagagtga aactgaggc cagcgccac tatgactgtc ctcaccgccc gggccgcat
 1200
 gagtacgcac tgcctttgac gcaactcagaa cctgagtatg ccacacctat cgtggagcgg
 1260
 cacctgctgc gagctcacac cttctccaca cagagcggct accgagctcc tgggcccagg
 1320
 cccactcacg aactcctcca ttctctgga ggctttctc ctgctacagg agccaccag
 1380
 gttgaaagct atcagaggcc agcaagccc aagcctgtgg gtggtggcta tgacaagcct
 1440
 gctgctagca gcttcttga cagcagagac ccagcctctc agtcacagat gacttccggg
 1500
 ggagatgatg gttattcggc acccagaaac ggtcttgcc cctcaacca gacggccatg
 1560
 actgctcttt tgtgaaccca atgtgaaaga aacctgctgt ggtactgagc ggcgaccgt
 1620
 gcgagtcact ggaagaaatg tgcaagcgtg catgtgtgac tcttcaggat cctagagacg
 1680
 acctcactta ctgtttacag aactgtgcag ctggtttagt tccaaccctt cctgcagagc
 1740
 cagttggttt ctgttgtgt agaacaagg gacttttctc atttgtctta actgtgatgc
 1800
 tgtgctgtaa aatgtgcaat ttgtacagtt atatttaaca cgaattaaca ttaaaaaaaaa
 1860
 aaaaaaaaaa a
 1871

<210> 44
 <211> 3767
 <212> DNA
 <213> Mouse

<400> 44
 cggacttggg gcgggaggct ggcgataaa aagccccag ggcgccccg gagggccgtt
 60
 agcgtgctc tgccgcgcg cccggcccag ccccgacct cacatcctgc cggcgtctg
 120
 aaatcaccat gatgtggccc caaccacca cttctccct gttcctgcta ctgctgctaa
 180
 gccaaagccc ttccagtagg ccacagtcac caggcaccaa gaagctcagg cttgtggggc
 240
 cagcggacag accaaaggag ggccgcttg aggtgctgca ccagggccag tggggcacgg
 300
 tgtgtgatga tgatttcgct ctccaggagg ctactgtggc ctgccgacag ctgggctttg
 360
 agtcagcctt gacctgggca cacagtgcc agtatggtca aggagagggc cccatctggc
 420
 tggacaatgt tcgttgtttg ggcaccgaga agaccctaga tcagtgtggc tctaacggct
 480
 ggggtatcag tgactgcaga cactcagaag atgttgggg ggtatgtcac ccacggcgcc
 540
 agcacggata tcaactctgag aaggtctcca atgccctcg gcctcagggc cggcggtag
 600
 aagaggtacg gctgaaaccc atcctcgcca gtgccaaaag gcacagccca gtgactgaa
 660

gggctgtgga agtacggtac gacggccact ggaggcaggt gtgtgaccag ggctggacca
720
tgaacaacag caggggttgta tgcgggatgc tgggctttcc cagtcagaca tctgtcaaca
780
gccactacta cagaaaagtc tggaatctga agatgaagga tcccaagtct aggctcaaca
840
gcctgacaaa aaagaattcc ttctggattc accgggttga ctgtttcggg acagagcccc
900
acttgccaa gtgccaggtc caggtggctc caggaagggg caagcttcgg gcagcctgtc
960
caggcggcat gcacgctgtg gtcagctgtg tggcagggcc ccacttcgc cgacagaagc
1020
caaagccac gcgcaaggag tcccatgcag aggagctgaa agtgcgctg cgctctgggg
1080
ctcaggtggg tgagggccgt gtggaagtgc tcatgaaccg ccagtggggc acagtctgtg
1140
accacaggtg gaacctcacc tcagccagcg tcgtgtgtcg ccagcttggc tttggctctg
1200
cccgggaggc cctttttggg gccagttgg gtcaagggtc aggaccacc cactgagtg
1260
agggtgcgctg ccgggggtat gagcggacc tgggtgactg ccttgccctg gaagggtccc
1320
agaatggttg tcaacatgca aacgacgctg ctgtcaggtg caacatccca gacatgggtc
1380
tccagaacaa ggtgcgcttg gctggtgggc gcaactccga agaggagtg gtggaggtgc
1440
agggtggaggt gaatggggtc ccacgatggg ggactgtatg cagtgaccac tgggggctca
1500
ccgaagccat ggtgacctgt cggcaacttg gtctgggatt tgccaacttt gctctcaagg
1560
acacctggta ctggcagggg acaccagagg ccaaagaagt ggtgatgagt ggagtctcgt
1620
gtcccgccac agaaatggcc ctgcagcagt gtcagaggca tgggcccgtg cactgttccc
1680
acggcccagg gcgcttctcg gctggcggtg cttgtatgaa cagtgtctca gacctcgtga
1740
tgaacgcccc gctggtacaa gagacggcgt acttgaggga tcgtccactc agcatgctgt
1800
actgtgtctc cgaggaaaac tgccctctcca agtccgctga tcacatggac tggccctacg
1860
ggtaccggcg cttgtctgcg ttctcctcac agatctacaa ccttggccgg gccgacttcc
1920
gtcccaaggc tggacgccac agctggattt ggcaccagtg ccacaggcac taccacagca
1980
tcgaagtctt cactcattat gacctgtctc cgctcaatgg ctccaagggt gccgagggac
2040
acaaggccag cttctgtcta gaagatacaa actgcccctc aggagtgcag cggcgctatg
2100
catgtgcaa ctttggggaa cagggagtggt ctgtaggctg ctgggacacc taccggcatg
2160
acatcgattg ccagtgggtg gatatacag atgtgggtcc aggggactat atcttccagg
2220
tggttgtgaa cccacaaaac gatgttcag agtccgattt ctccaataac atgatacgtg
2280
gccgtgcaa gtatgatgga cagcgagtct ggttgcaaa ctgccacaca ggagattcct
2340
accgagccaa tgcagagctc tccctggagc aggaacagcg actcaggaac aacttgatct
2400
gaagccatta ctgcactccc agctctgctc acacaccaga tacctcagct gactggagcc
2460
atgcccttca caaagccctg actcacagga caaggggcta gtgacaagga gcaccaagaa
2520
gctgctcagg aggcctttca gtggccagat catcaccgg gatggcagtt ctctcaggat
2580
ggctctgggc cagctcaacc ttctcttctc tcaggagact cgatcttctt tacaacttga
2640

tgcacagttc ccagtttcag gagctctaag ttcctcaggg atgaactgtg accaaggccc
 2700
 cctctaagtg gtgctttgca aatgtcttgg aggaccaaag gacagacgac ccgagaacac
 2760
 aagctgtgga tggagtcggt ttctctgcta tacgtccac gcaaaaggac catgtcaaag
 2820
 tcacacctgg cagagacgct ggtgaacaca gtccctcagc ttaccctcac ttagaactcg
 2880
 catctcaggc tctgaagcct ctccctgcat ctttaccttc attcggtcac acatggtggt
 2940
 tccaatatcc ctgaaccctc aggcctcctc catttcctga tgggtcaaca cctcgattat
 3000
 tggggctggg gagcaagttt cacagaatga cgagacaggg cctttcctgc agagtagtca
 3060
 gaaagcaaga cgaaggctga ggtcacatga attcagcctc ggaggacctc tgcccaggga
 3120
 ggtgccatat ctggcaggca ggccagtctc ttagaatcac ccacattgta gggtagcct
 3180
 aaatttcaga tttaaccaaa gccacttcac cttaaacttt tgcaattgag aagaaattgg
 3240
 tcagccaagc ccctctgcag gaacaccaag acagggtccag tagagttagg aacagaagac
 3300
 ggagttaaca agaagtgaga aggaaacctg ggagaggcca ccatccagtg aggcggctgt
 3360
 gctctgttct tgctcaggtg gtataagacc tggagtcttc cagggcatgc ctggaccttt
 3420
 tctccactga catacacaca gatgatcctt ctaggtctta taatgccaac aaaggttgc
 3480
 cactatgggc tgccacaaag gccagaccag ctgagcttct gcagcttcca ctgcactaca
 3540
 ctctgccctc ttccctocag agctggatga cgctcggaac acaatccttg gcacagccca
 3600
 ccctagtaca tttcttgggt ctcacactaa cctgcttcac cgttacgtg cccaaggtea
 3660
 acagtgaatc ttgggtcagg aaggctgaga ggtgaagggg aggaatgaga aggtgtgacc
 3720
 cagactttag acttttataa cagaggctac aaaaaaaaaa aaaaaaa
 3767

<210> 45
 <211> 925
 <212> DNA
 <213> Mouse

<400> 45
 gcgcgcgcgg cgatggaggc ggcggcgacc gtggttttgg ccctggcgct gtcgggggcc
 60
 ggcgcgcggg gcgcggcgag tgacgacttc aacctgggag acgccctgga ggacccaac
 120
 atgaagccaa cccccaaggc cccaacgccc aagaagccgt caggaggctt cgacctggag
 180
 gacgcctcgc ccggcggcgg cgaggaggc gcaggagaga agccgggaaa ccggcccgag
 240
 ccggacccga agccgccaa ggcacacgga gactcaggcg gcatctcgga cagcgacctg
 300
 gcagacgccg ccggccaggg aggcggagcc gggcgacgcg ggagcggaga cgaaggcggc
 360
 catggcggcg ctggcggggc ggagccggaa gggacgcccc agggcttggg gccggcgctg
 420
 gtggcgcccg ttgtggccgc cgtggcgggc gcggtgtcga gcttcgtggc ctatcagcgg
 480
 cggcgccgtg gcttcgcgga gggcggtcc gccccgtgt agatgacgcc atggccccgc
 540
 cctccgggc atcatcgccc cctccagggc cccgatgaca tcaactgacgc tgctcatttg
 600
 catacgcgct ccggcccgct gtgacgtcac tgaccccgcc cccggcctcg cctgaatatg

660
 caaatagtcg gccccgcctc ccgccgtgaa atcaccgcct gcaccgcccc tcgccgctgc
 720
 atcagtgatg tcaactactgc caaagactcc gccacaaact gacctctgac cccggtgaca
 780
 tcataacctc cactcacaag gagccatcat gggcagcccc ctgtctcagc tcagcatccc
 840
 ctccaggaca ggaaggggag gagcctgaag gccgggggag ggaccggaaa taaaggcgga
 900
 gttttgtaaa aaaaaaaaaa aaaaa
 925

<210> 46
 <211> 1423
 <212> DNA
 <213> Mouse

<400> 46
 tctgtgcggc tcaagtgtgt ggccagtggg caccacggc cagacatcat gtggatgaag
 60
 gatgaccaga ccttgacgca tctagaggct agtgaacaca gaaagaagaa gtggacactg
 120
 agcctgaaga acctgaagcc tgaagacagt ggcaagtaca cgtgccgtgt atctaacaag
 180
 gccggtgcc tcaacgccac ctacaaagtgt gatgtaatcc gtgagtgggt ggtctgtggt
 240
 aggacagggg cccgtggtgc ctaaaactgt gctgacatgt ttgtttttcc ttggcttaga
 300
 gcggactcgt tccaagcctg tgctcacagg gacacaccct gtgaacacaa cgggtggactt
 360
 cgggtgggaca acgtccttcc agtgcaaggt gcgcagtgc gtgaagcctg tgatccagt
 420
 gctgaagcgg gtggagtacg gctccgaggg acgccacaac tccaccattg atgtgggtgg
 480
 ccagaagttt gtggtgttgc ccacgggtga tgtgtgttca cggcctgatg gctcctacct
 540
 caacaagctg ctcatctctc gggcccgcca ggatgatgct ggcattgaca tctgcctagg
 600
 tgcaaatacc atgggctaca gtttccgtag cgccttctc actgtattac cagggtgtgtg
 660
 tgtgggctgc ccaccccatg tttactctca gtctctacca ttgggtctggg ctgtcctggg
 720
 gttccccaat gtccacttag caagtggggc ctccctatcc ttttcccttc gttgtgggtt
 780
 atccttgctt catagggagt tcaggggtgc tgcccatata gttcacattt gggtggtt
 840
 cccattaat ataggacat tctgtccctt actcttcttc ttaattcttc ttgcagaccc
 900
 caaacctcca gggcctccta tggcttcttc atcgtcatcc acaagcctgc catggcctgt
 960
 ggtgatcggc atcccagctg gtgctgtctt catcctaggc actgtgctgc tctggctttg
 1020
 ccagaccaag aagaagccat gtgcccagc atctacactt cctgtgcctg ggcattgctc
 1080
 cccagggaca tcccagaaac gcagtgttga caaggacctg cctcattgg ctgtgggcat
 1140
 atgtgaggag catggatccg ccatggcccc ccagcacatc ctggcctctg gctcaactgc
 1200
 tggccccaag ctgtacccca agctatacac agatgtgcac acacacacac atacacacac
 1260
 ctgactcac acgtctctcat gtggagggca aggttcatca acaccagcat gtccactatc
 1320
 agtgctaaat acagcgaatc tccaagcact gtgtcctgag gtaggcatat gggggccaag
 1380
 gcaacagggt gggagaattg agaacaatgg aggaagagta tct
 1423

<210> 47
 <211> 464
 <212> PRT
 <213> Mouse

<400> 47
 Met Gly Arg Ala Trp Gly Leu Leu Val Gly Leu Leu Gly Val Val Trp
 1 5 10 15
 Leu Leu Arg Leu Gly His Gly Glu Glu Arg Arg Pro Glu Thr Ala Ala
 20 25 30
 Gln Arg Cys Phe Cys Gln Val Ser Gly Tyr Leu Asp Asp Cys Thr Cys
 35 40 45
 Asp Val Glu Thr Ile Asp Lys Phe Asn Asn Tyr Arg Leu Phe Pro Arg
 50 55 60
 Leu Gln Lys Leu Leu Glu Ser Asp Tyr Phe Arg Tyr Tyr Lys Val Asn
 65 70 75 80
 Leu Lys Lys Pro Cys Pro Phe Trp Asn Asp Ile Asn Gln Cys Gly Arg
 85 90 95
 Arg Asp Cys Ala Val Lys Pro Cys His Ser Asp Glu Val Pro Asp Gly
 100 105 110
 Ile Lys Ser Ala Ser Tyr Lys Tyr Ser Glu Glu Ala Asn Arg Ile Glu
 115 120 125
 Glu Cys Glu Gln Ala Glu Arg Leu Gly Ala Val Asp Glu Ser Leu Ser
 130 135 140
 Glu Glu Thr Gln Lys Ala Val Leu Gln Trp Thr Lys His Asp Asp Ser
 145 150 155 160
 Ser Asp Ser Phe Cys Glu Ile Asp Asp Ile Gln Ser Pro Asp Ala Glu
 165 170 175
 Tyr Val Asp Leu Leu Leu Asn Pro Glu Arg Tyr Thr Gly Tyr Lys Gly
 180 185 190
 Pro Asp Ala Trp Arg Ile Trp Ser Val Ile Tyr Glu Glu Asn Cys Phe
 195 200 205
 Lys Pro Gln Thr Ile Gln Arg Pro Leu Ala Ser Gly Arg Gly Lys Ser
 210 215 220
 Lys Glu Asn Thr Phe Tyr Asn Trp Leu Glu Gly Leu Cys Val Glu Lys
 225 230 235 240
 Arg Ala Phe Tyr Arg Leu Ile Ser Gly Leu His Ala Ser Ile Asn Val
 245 250 255
 His Leu Ser Ala Arg Tyr Leu Leu Gln Asp Thr Trp Leu Glu Lys Lys
 260 265 270
 Trp Gly His Asn Val Thr Glu Phe Gln Gln Arg Phe Asp Gly Ile Leu
 275 280 285
 Thr Glu Gly Glu Gly Pro Arg Arg Leu Arg Asn Leu Tyr Phe Leu Tyr
 290 295 300
 Leu Ile Glu Leu Arg Ala Leu Ser Lys Val Leu Pro Phe Phe Glu Arg
 305 310 315 320
 Pro Asp Phe Gln Leu Phe Thr Gly Asn Lys Val Gln Asp Ala Glu Asn
 325 330 335
 Lys Ala Leu Leu Leu Glu Ile Leu His Glu Ile Lys Ser Phe Pro Leu
 340 345 350
 His Phe Asp Glu Asn Ser Phe Phe Ala Gly Asp Lys Asn Glu Ala His
 355 360 365
 Lys Leu Lys Glu Asp Phe Arg Leu His Phe Arg Asn Ile Ser Arg Ile
 370 375 380
 Met Asp Cys Val Gly Cys Phe Lys Cys Arg Leu Trp Gly Lys Leu Gln
 385 390 395 400
 Thr Gln Gly Leu Gly Thr Ala Leu Lys Ile Leu Phe Ser Glu Lys Leu
 405 410 415
 Ile Ala Asn Met Pro Glu Ser Gly Pro Ser Tyr Glu Phe Gln Leu Thr
 420 425 430
 Arg Gln Glu Ile Val Ser Leu Phe Asn Ala Phe Gly Arg Ile Ser Thr
 435 440 445
 Ser Val Arg Glu Leu Glu Asn Phe Arg His Leu Leu Gln Asn Val His
 450 455 460

<210> 48
 <211> 664
 <212> PRT
 <213> Mouse

<400> 48
 Met Lys Arg Arg Asn Ala Asp Cys Ser Lys Leu Arg Arg Pro Leu Lys
 1 5 10 15
 Arg Asn Arg Ile Thr Glu Gly Ile Tyr Gly Ser Thr Phe Leu Tyr Leu
 20 25 30
 Lys Phe Leu Val Val Trp Ala Leu Val Leu Leu Ala Asp Phe Val Leu
 35 40 45
 Glu Phe Arg Phe Glu Tyr Leu Trp Pro Phe Trp Leu Phe Ile Arg Ser
 50 55 60
 Val Tyr Asp Ser Phe Arg Tyr Gln Gly Leu Ala Phe Ser Val Phe Phe
 65 70 75 80
 Val Cys Val Ala Phe Thr Ser Asn Ile Ile Cys Leu Leu Phe Ile Pro
 85 90 95
 Ile Gln Trp Leu Phe Phe Ala Ala Ser Thr Tyr Val Trp Val Gln Tyr
 100 105 110
 Val Trp His Thr Glu Arg Gly Val Cys Leu Pro Thr Val Ser Leu Trp
 115 120 125
 Ile Leu Phe Val Tyr Ile Glu Ala Ala Ile Arg Phe Lys Asp Leu Lys
 130 135 140
 Asn Phe His Val Asp Leu Cys Arg Pro Phe Ala Ala His Cys Ile Gly
 145 150 155 160
 Tyr Pro Val Val Thr Leu Gly Phe Gly Phe Lys Ser Tyr Val Ser Tyr
 165 170 175
 Lys Met Arg Leu Arg Lys Gln Lys Glu Val Gln Lys Glu Asn Glu Phe
 180 185 190
 Tyr Met Gln Leu Leu Gln Gln Ala Leu Pro Pro Glu Gln Gln Met Leu
 195 200 205
 Gln Lys Gln Glu Lys Glu Ala Glu Glu Ala Ala Lys Gly Leu Pro Asp
 210 215 220
 Met Asp Ser Ser Ile Leu Ile His His Asn Gly Gly Ile Pro Ala Asn
 225 230 235 240
 Lys Lys Leu Ser Thr Thr Leu Pro Glu Ile Glu Tyr Arg Glu Lys Gly
 245 250 255
 Lys Glu Lys Asp Lys Asp Ala Lys Lys His Asn Leu Gly Ile Asn Asn
 260 265 270
 Asn Asn Ile Leu Gln Pro Val Asp Ser Lys Ile Gln Glu Ile Glu Tyr
 275 280 285
 Met Glu Asn His Ile Asn Ser Lys Arg Leu Asn Asn Asp Leu Val Gly
 290 295 300
 Ser Thr Glu Asn Leu Leu Lys Glu Asp Ser Cys Thr Ala Ser Ser Lys
 305 310 315 320
 Asn Tyr Lys Asn Ala Ser Gly Val Val Asn Ser Ser Pro Arg Ser His
 325 330 335
 Ser Ala Thr Asn Gly Ser Ile Pro Ser Ser Ser Ser Lys Asn Glu Lys
 340 345 350
 Lys Gln Lys Cys Thr Ser Lys Gly Pro Ser Ala His Lys Asp Leu Met
 355 360 365
 Glu Asn Cys Ile Pro Asn Asn Gln Leu Ser Lys Pro Asp Ala Leu Val
 370 375 380
 Arg Leu Glu Gln Asp Ile Lys Lys Leu Lys Ala Asp Leu Gln Ala Ser
 385 390 395 400
 Arg Gln Val Glu Gln Glu Leu Arg Ser Gln Ile Ser Ala Leu Ser Ser
 405 410 415
 Thr Glu Arg Gly Ile Arg Ser Glu Met Gly Gln Leu Arg Gln Glu Asn
 420 425 430
 Glu Leu Leu Gln Asn Lys Leu His Asn Ala Val Gln Met Lys Gln Lys
 435 440 445
 Asp Lys Gln Asn Ile Ser Gln Leu Glu Lys Lys Leu Lys Ala Glu Gln
 450 455 460
 Glu Ala Arg Ser Phe Val Glu Lys Gln Leu Met Glu Glu Lys Lys Arg
 465 470 475 480

Lys Lys Leu Glu Glu Ala Thr Ala Ala Arg Ala Val Ala Phe Ala Ala
 485 490 495
 Ala Ser Arg Gly Glu Cys Thr Glu Thr Leu Arg Ser Arg Ile Arg Glu
 500 505 510
 Leu Glu Ala Glu Gly Lys Lys Leu Thr Met Asp Met Lys Val Lys Glu
 515 520 525
 Glu Gln Ile Arg Glu Leu Glu Leu Lys Val Gln Glu Leu Arg Lys Tyr
 530 535 540
 Lys Glu Asn Glu Lys Asp Thr Glu Val Leu Met Ser Ala Leu Ser Ala
 545 550 555 560
 Met Gln Asp Lys Thr Gln His Leu Glu Asn Ser Leu Ser Ala Glu Thr
 565 570 575
 Arg Ile Lys Leu Asp Leu Phe Ser Ala Leu Gly Asp Ala Lys Arg Gln
 580 585 590
 Leu Glu Ile Ala Gln Gly Gln Ile Leu Gln Lys Asp Gln Glu Ile Lys
 595 600 605
 Asp Leu Lys Gln Lys Ile Ala Glu Val Met Ala Val Met Pro Ser Ile
 610 615 620
 Thr Tyr Ser Ala Ala Thr Ser Pro Leu Ser Pro Val Ser Pro His Tyr
 625 630 635 640
 Ser Ser Lys Phe Val Glu Thr Ser Pro Ser Gly Leu Asp Pro Asn Ala
 645 650 655
 Ser Val Tyr Gln Pro Leu Lys Lys
 660

<210> 49
 <211> 199
 <212> PRT
 <213> Mouse

<400> 49
 Met Ala Ser Leu Trp Cys Gly Asn Leu Leu Arg Leu Gly Ser Gly Leu
 1 5 10 15
 Asn Met Ser Cys Leu Ala Leu Ser Val Leu Leu Leu Ala Gln Leu Thr
 20 25 30
 Gly Ala Ala Lys Asn Phe Glu Asp Val Arg Cys Lys Cys Ile Cys Pro
 35 40 45
 Pro Tyr Lys Glu Asn Pro Gly His Ile Tyr Asn Lys Asn Ile Ser Gln
 50 55 60
 Lys Asp Cys Asp Cys Leu His Val Val Glu Pro Met Pro Val Arg Gly
 65 70 75 80
 Pro Asp Val Glu Ala Tyr Cys Leu Arg Cys Glu Cys Lys Tyr Glu Glu
 85 90 95
 Arg Ser Ser Val Thr Ile Lys Val Thr Ile Ile Ile Tyr Leu Ser Ile
 100 105 110
 Leu Gly Leu Leu Leu Leu Tyr Met Val Tyr Leu Thr Leu Val Glu Pro
 115 120 125
 Ile Leu Lys Arg Arg Leu Phe Gly His Ser Gln Leu Leu Gln Ser Asp
 130 135 140
 Asp Asp Val Gly Asp His Gln Pro Phe Ala Asn Ala His Asp Val Leu
 145 150 155 160
 Ala Arg Ser Arg Ser Arg Ala Asn Val Leu Asn Lys Val Glu Tyr Ala
 165 170 175
 Gln Gln Arg Trp Lys Leu Gln Val Gln Glu Gln Arg Lys Ser Val Phe
 180 185 190
 Asp Arg His Val Val Leu Ser
 195

<210> 50
 <211> 227
 <212> PRT
 <213> Mouse

<400> 50
 Met Gly Pro Leu His Gln Phe Leu Leu Leu Leu Ile Thr Ala Leu Ser
 1 5 10 15

Gln Ala Leu Asn Thr Thr Val Leu Gln Gly Met Ala Gly Gln Ser Leu
 20 25 30
 Arg Val Ser Cys Thr Tyr Asp Ala Leu Lys His Trp Gly Arg Arg Lys
 35 40 45
 Ala Trp Cys Arg Gln Leu Gly Glu Glu Gly Pro Cys Gln Arg Val Val
 50 55 60
 Ser Thr His Gly Val Trp Leu Leu Ala Phe Leu Lys Lys Arg Asn Gly
 65 70 75 80
 Ser Thr Val Ile Ala Asp Asp Thr Leu Ala Gly Thr Val Thr Ile Thr
 85 90 95
 Leu Lys Asn Leu Gln Ala Gly Asp Ala Gly Leu Tyr Gln Cys Gln Ser
 100 105 110
 Leu Arg Gly Arg Glu Ala Glu Val Leu Gln Lys Val Leu Val Glu Val
 115 120 125
 Leu Glu Asp Pro Leu Asp Asp Gln Asp Ala Gly Asp Leu Trp Val Pro
 130 135 140
 Glu Glu Ser Ser Ser Phe Glu Gly Ala Gln Val Glu His Ser Thr Ser
 145 150 155 160
 Arg Asn Gln Glu Thr Ser Phe Pro Pro Thr Ser Ile Leu Leu Leu Leu
 165 170 175
 Ala Cys Val Leu Leu Ser Lys Phe Leu Ala Ala Ser Ile Leu Trp Ala
 180 185 190
 Val Ala Arg Gly Arg Gln Lys Pro Gly Thr Pro Val Val Arg Gly Leu
 195 200 205
 Asp Cys Gly Gln Asp Ala Gly His Gln Leu Gln Ile Leu Thr Gly Pro
 210 215 220
 Gly Gly Thr
 225

<210> 51
 <211> 503
 <212> PRT
 <213> Mouse

<400> 51
 Met Gly Thr Gly Ala Gly Gly Pro Ser Val Leu Ala Leu Leu Phe Ala
 1 5 10 15
 Val Cys Ala Pro Leu Arg Leu Gln Ala Glu Glu Leu Gly Asp Gly Cys
 20 25 30
 Gly His Ile Val Thr Ser Gln Asp Ser Gly Thr Met Thr Ser Lys Asn
 35 40 45
 Tyr Pro Gly Thr Tyr Pro Asn Tyr Thr Val Cys Glu Lys Ile Ile Thr
 50 55 60
 Val Pro Lys Gly Lys Arg Leu Ile Leu Arg Leu Gly Asp Leu Asn Ile
 65 70 75 80
 Glu Ser Lys Thr Cys Ala Ser Asp Tyr Leu Leu Phe Ser Ser Ala Thr
 85 90 95
 Asp Gln Tyr Gly Pro Tyr Cys Gly Ser Trp Ala Val Pro Lys Glu Leu
 100 105 110
 Arg Leu Asn Ser Asn Glu Val Thr Val Leu Phe Lys Ser Gly Ser His
 115 120 125
 Ile Ser Gly Arg Gly Phe Leu Leu Thr Tyr Ala Ser Ser Asp His Pro
 130 135 140
 Asp Leu Ile Thr Cys Leu Glu Arg Gly Ser His Tyr Phe Glu Glu Lys
 145 150 155 160
 Tyr Ser Lys Phe Cys Pro Ala Gly Cys Arg Asp Ile Ala Arg Asp Ile
 165 170 175
 Ser Gly Asn Thr Lys Asp Gly Tyr Arg Asp Thr Ser Leu Leu Cys Lys
 180 185 190
 Ala Ala Ile His Ala Gly Ile Ile Thr Asp Glu Leu Gly Gly His Ile
 195 200 205
 Asn Leu Leu Gln Ser Lys Gly Ile Ser His Tyr Glu Gly Leu Leu Ala
 210 215 220
 Asn Gly Val Leu Ser Arg His Gly Ser Leu Ser Glu Lys Arg Phe Leu
 225 230 235 240
 Phe Thr Thr Pro Gly Met Asn Ile Thr Thr Val Ala Ile Pro Ser Val

Ile	Phe	Ile	Ala	245	Leu	Leu	Leu	Thr	Gly	250	Met	Gly	Ile	Phe	Ala	255	Ile	Cys
			260						265							270		
Arg	Lys	Arg	Lys	Lys	Lys	Gly	Asn	Pro	Tyr	Val	Ser	Ala	Asp	Ala	Gln			
		275					280							285				
Lys	Thr	Gly	Cys	Trp	Lys	Gln	Ile	Lys	Tyr	Pro	Phe	Ala	Arg	His	Gln			
		290					295						300					
Ser	Thr	Glu	Phe	Thr	Ile	Ser	Tyr	Asp	Asn	Glu	Lys	Glu	Met	Thr	Gln			
305					310					315					320			
Lys	Leu	Asp	Leu	Ile	Thr	Ser	Asp	Met	Ala	Asp	Tyr	Gln	Gln	Pro	Leu			
				325					330					335				
Met	Ile	Gly	Thr	Gly	Thr	Val	Ala	Arg	Lys	Gly	Ser	Thr	Phe	Arg	Pro			
			340						345					350				
Met	Asp	Thr	Asp	Thr	Glu	Glu	Val	Arg	Val	Asn	Thr	Glu	Ala	Ser	Gly			
			355					360					365					
His	Tyr	Asp	Cys	Pro	His	Arg	Pro	Gly	Arg	His	Glu	Tyr	Ala	Leu	Pro			
370						375					380							
Leu	Thr	His	Ser	Glu	Pro	Glu	Tyr	Ala	Thr	Pro	Ile	Val	Glu	Arg	His			
385					390					395					400			
Leu	Leu	Arg	Ala	His	Thr	Phe	Ser	Thr	Gln	Ser	Gly	Tyr	Arg	Val	Pro			
				405					410					415				
Gly	Pro	Arg	Pro	Thr	His	Glu	His	Ser	His	Ser	Ser	Gly	Gly	Phe	Pro			
			420					425					430					
Pro	Ala	Thr	Gly	Ala	Thr	Gln	Val	Glu	Ser	Tyr	Gln	Arg	Pro	Ala	Ser			
			435					440				445						
Pro	Lys	Pro	Val	Gly	Gly	Gly	Tyr	Asp	Lys	Pro	Ala	Ala	Ser	Ser	Phe			
			450			455					460							
Leu	Asp	Ser	Arg	Asp	Pro	Ala	Ser	Gln	Ser	Gln	Met	Thr	Ser	Gly	Gly			
465					470					475					480			
Asp	Asp	Gly	Tyr	Ser	Ala	Pro	Arg	Asn	Gly	Leu	Ala	Pro	Leu	Asn	Gln			
				485					490					495				
Thr	Ala	Met	Thr	Ala	Leu	Leu												
				500														

<210> 52
 <211> 757
 <212> PRT
 <213> Mouse

				<400>	52													
Met	Met	Trp	Pro	Gln	Pro	Pro	Thr	Phe	Ser	Leu	Phe	Leu	Leu	Leu	Leu			
1				5					10					15				
Leu	Ser	Gln	Ala	Pro	Ser	Ser	Arg	Pro	Gln	Ser	Ser	Gly	Thr	Lys	Lys			
			20					25					30					
Leu	Arg	Leu	Val	Gly	Pro	Ala	Asp	Arg	Pro	Lys	Glu	Gly	Arg	Leu	Glu			
			35				40					45						
Val	Leu	His	Gln	Gly	Gln	Trp	Gly	Thr	Val	Cys	Asp	Asp	Asp	Phe	Ala			
			50			55					60							
Leu	Gln	Glu	Ala	Thr	Val	Ala	Cys	Arg	Gln	Leu	Gly	Phe	Glu	Ser	Ala			
65					70					75				80				
Leu	Thr	Trp	Ala	His	Ser	Ala	Lys	Tyr	Gly	Gln	Gly	Glu	Gly	Pro	Ile			
				85					90					95				
Trp	Leu	Asp	Asn	Val	Arg	Cys	Leu	Gly	Thr	Glu	Lys	Thr	Leu	Asp	Gln			
			100					105					110					
Cys	Gly	Ser	Asn	Gly	Trp	Gly	Ile	Ser	Asp	Cys	Arg	His	Ser	Glu	Asp			
			115				120					125						
Val	Gly	Val	Val	Cys	His	Pro	Arg	Arg	Gln	His	Gly	Tyr	His	Ser	Glu			
			130			135					140							
Lys	Val	Ser	Asn	Ala	Leu	Gly	Pro	Gln	Gly	Arg	Arg	Leu	Glu	Glu	Val			
145				150					155					160				
Arg	Leu	Lys	Pro	Ile	Leu	Ala	Ser	Ala	Lys	Arg	His	Ser	Pro	Val	Thr			
				165					170					175				
Glu	Gly	Ala	Val	Glu	Val	Arg	Tyr	Asp	Gly	His	Trp	Arg	Gln	Val	Cys			
			180					185					190					
Asp	Gln	Gly	Trp	Thr	Met	Asn	Asn	Ser	Arg	Val	Val	Cys	Gly	Met	Leu			
			195				200						205					

Gly	Phe	Pro	Ser	Gln	Thr	Ser	Val	Asn	Ser	His	Tyr	Tyr	Arg	Lys	Val
210						215					220				
Trp	Asn	Leu	Lys	Met	Lys	Asp	Pro	Lys	Ser	Arg	Leu	Asn	Ser	Leu	Thr
225					230					235					240
Lys	Lys	Asn	Ser	Phe	Trp	Ile	His	Arg	Val	Asp	Cys	Phe	Gly	Thr	Glu
				245					250					255	
Pro	His	Leu	Ala	Lys	Cys	Gln	Val	Gln	Val	Ala	Pro	Gly	Arg	Gly	Lys
			260					265					270		
Leu	Arg	Ala	Ala	Cys	Pro	Gly	Gly	Met	His	Ala	Val	Val	Ser	Cys	Val
		275				280						285			
Ala	Gly	Pro	His	Phe	Arg	Arg	Gln	Lys	Pro	Lys	Pro	Thr	Arg	Lys	Glu
290					295						300				
Ser	His	Ala	Glu	Glu	Leu	Lys	Val	Arg	Leu	Arg	Ser	Gly	Ala	Gln	Val
305					310					315					320
Gly	Glu	Gly	Arg	Val	Glu	Val	Leu	Met	Asn	Arg	Gln	Trp	Gly	Thr	Val
			325					330						335	
Cys	Asp	His	Arg	Trp	Asn	Leu	Ile	Ser	Ala	Ser	Val	Val	Cys	Arg	Gln
			340					345					350		
Leu	Gly	Phe	Gly	Ser	Ala	Arg	Glu	Ala	Leu	Phe	Gly	Ala	Gln	Leu	Gly
		355					360					365			
Gln	Gly	Leu	Gly	Pro	Ile	His	Leu	Ser	Glu	Val	Arg	Cys	Arg	Gly	Tyr
370					375						380				
Glu	Arg	Thr	Leu	Gly	Asp	Cys	Leu	Ala	Leu	Glu	Gly	Ser	Gln	Asn	Gly
385					390					395					400
Cys	Gln	His	Ala	Asn	Asp	Ala	Ala	Val	Arg	Cys	Asn	Ile	Pro	Asp	Met
			405					410						415	
Gly	Phe	Gln	Asn	Lys	Val	Arg	Leu	Ala	Gly	Gly	Arg	Asn	Ser	Glu	Glu
			420					425					430		
Gly	Val	Val	Glu	Val	Gln	Val	Glu	Val	Asn	Gly	Val	Pro	Arg	Trp	Gly
		435					440					445			
Thr	Val	Cys	Ser	Asp	His	Trp	Gly	Leu	Thr	Glu	Ala	Met	Val	Thr	Cys
450					455						460				
Arg	Gln	Leu	Gly	Leu	Gly	Phe	Ala	Asn	Phe	Ala	Leu	Lys	Asp	Thr	Trp
465					470					475					480
Tyr	Trp	Gln	Gly	Thr	Pro	Glu	Ala	Lys	Glu	Val	Val	Met	Ser	Gly	Val
			485						490					495	
Arg	Cys	Ser	Gly	Thr	Glu	Met	Ala	Leu	Gln	Gln	Cys	Gln	Arg	His	Gly
			500					505					510		
Pro	Val	His	Cys	Ser	His	Gly	Pro	Gly	Arg	Phe	Ser	Ala	Gly	Val	Ala
		515					520					525			
Cys	Met	Asn	Ser	Ala	Pro	Asp	Leu	Val	Met	Asn	Ala	Gln	Leu	Val	Gln
530					535						540				
Glu	Thr	Ala	Tyr	Leu	Glu	Asp	Arg	Pro	Leu	Ser	Met	Leu	Tyr	Cys	Ala
545					550					555					560
His	Glu	Glu	Asn	Cys	Leu	Ser	Lys	Ser	Ala	Asp	His	Met	Asp	Trp	Pro
			565					570					575		
Tyr	Gly	Tyr	Arg	Arg	Leu	Leu	Arg	Phe	Ser	Ser	Gln	Ile	Tyr	Asn	Leu
			580					585					590		
Gly	Arg	Ala	Asp	Phe	Arg	Pro	Lys	Ala	Gly	Arg	His	Ser	Trp	Ile	Trp
		595				600						605			
His	Gln	Cys	His	Arg	His	Tyr	His	Ser	Ile	Glu	Val	Phe	Thr	His	Tyr
610					615						620				
Asp	Leu	Leu	Thr	Leu	Asn	Gly	Ser	Lys	Val	Ala	Glu	Gly	His	Lys	Ala
625					630					635					640
Ser	Phe	Cys	Leu	Glu	Asp	Thr	Asn	Cys	Pro	Ser	Gly	Val	Gln	Arg	Arg
			645					650					655		
Tyr	Ala	Cys	Ala	Asn	Phe	Gly	Glu	Gln	Gly	Val	Ala	Val	Gly	Cys	Trp
		660				665						670			
Asp	Thr	Tyr	Arg	His	Asp	Ile	Asp	Cys	Gln	Trp	Val	Asp	Ile	Thr	Asp
		675				680						685			
Val	Gly	Pro	Gly	Asp	Tyr	Ile	Phe	Gln	Val	Val	Val	Asn	Pro	Thr	Asn
690					695						700				
Asp	Val	Ala	Glu	Ser	Asp	Phe	Ser	Asn	Asn	Met	Ile	Arg	Cys	Arg	Cys
705					710					715					720
Lys	Tyr	Asp	Gly	Gln	Arg	Val	Trp	Leu	His	Asn	Cys	His	Thr	Gly	Asp
			725					730						735	

Ser Tyr Arg Ala Asn Ala Glu Leu Ser Leu Glu Gln Glu Gln Arg Leu
 740 745 750
 Arg Asn Asn Leu Ile
 755

<210> 53
 <211> 169
 <212> PRT
 <213> Mouse

<400> 53
 Met Glu Ala Ala Thr Val Val Leu Ala Leu Ala Leu Leu Gly Ala
 1 5 10 15
 Ala Ala Arg Gly Ala Ala Ser Asp Asp Phe Asn Leu Gly Asp Ala Leu
 20 25 30
 Glu Asp Pro Asn Met Lys Pro Thr Pro Lys Ala Pro Thr Pro Lys Lys
 35 40 45
 Pro Ser Gly Gly Phe Asp Leu Glu Asp Ala Leu Pro Gly Gly Gly Gly
 50 55 60
 Gly Gly Ala Gly Glu Lys Pro Gly Asn Arg Pro Gln Pro Asp Pro Lys
 65 70 75 80
 Pro Pro Arg Pro His Gly Asp Ser Gly Gly Ile Ser Asp Ser Asp Leu
 85 90 95
 Ala Asp Ala Ala Gly Gln Gly Gly Gly Ala Gly Arg Arg Gly Ser Gly
 100 105 110
 Asp Glu Gly Gly His Gly Gly Ala Gly Gly Ala Glu Pro Glu Gly Thr
 115 120 125
 Pro Gln Gly Leu Val Pro Gly Val Val Ala Ala Val Val Ala Ala Val
 130 135 140
 Ala Gly Ala Val Ser Ser Phe Val Ala Tyr Gln Arg Arg Arg Leu Cys
 145 150 155 160
 Phe Arg Glu Gly Gly Ser Ala Pro Val
 165

<210> 54
 <211> 30
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 54
 cccaagctta tgacgcggag ccccgcgctg
 30

<210> 55
 <211> 35
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 55
 cgggatccag gccatggcag gcttgtggat gacga
 35

<210> 56
 <211> 37
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 56
ccgctcgagt agatactott cctccattgt tctcatt
37

<210> 57
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 57
ctgtgcggct caagtgtg
18

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ00/00015

A. CLASSIFICATION OF SUBJECT MATTER												
Int. Cl. ⁷ : C12N 15/12												
According to International Patent Classification (IPC) or to both national classification and IPC												
B. FIELDS SEARCHED												
Minimum documentation searched (classification system followed by classification symbols) AS ABOVE												
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched AS BELOW												
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) GenPept, Swiss Prot, TREMBL, PIR												
C. DOCUMENTS CONSIDERED TO BE RELEVANT												
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.										
P(X)	Gen Pept Acc no CAB90552	SEQ ID NO 12										
X	Gen Pept Acc no AAC78827	SEQ ID NO 16										
X	Gen Pept Acc no AAC64321	SEQ ID NO 20										
X	Gen Pept Acc no AAD09175											
X	Gen Pept Acc no AAB30638											
X	Gen Pept Acc no CAA53271	SEQ ID NOs 31 & 32										
X	PIR Acc no S38579											
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <input type="checkbox"/> See patent family annex												
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td> </tr> <tr> <td>"E" earlier application or patent but published on or after the international filing date</td> <td>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td> </tr> <tr> <td>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td> <td>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention											
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone											
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art											
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family											
"P" document published prior to the international filing date but later than the priority date claimed												
Date of the actual completion of the international search 26 May 2000		Date of mailing of the international search report 19 JUN 2000										
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustalia.gov.au Facsimile No. (02) 6285 3929		Authorized officer GILLIAN ALLEN Telephone No : (02) 6283 2266										

INTERNATIONAL SEARCH REPORT

International application No.

PCT/NZ00/00015

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GenPept acc no CAA41209	SEQ ID NO 33
X	GenPept acc no AAB25535	SEQ ID NO 33
P(X)	Swiss Prot acc no Q99969	SEQ ID NOs 34 & 35
P(X)	GenPept acc no CAB65272	SEQ ID NO 36
P(X)	GenPept acc no AAF03400	SEQ ID NO 36
X	Swiss Prot acc no Q14956	SEQ ID NO 36
X(P)	GenPept acc no CAB65272	SEQ ID NO 37
X(P)	PIR acc no T17265	SEQ ID NO 37
X	Swiss Prot acc no P53104	SEQ ID NO 37
P(X)	GenPept acc no CAB65272	SEQ ID NO 36
X	Swiss Prot acc no Q14956	SEQ ID NO 36
X	Swiss Prot acc no P14730	SEQ ID NO 38
P(X)	GenPept acc no AAF20364	SEQ ID NO 47
P(X)	GenPept acc no BAA91786	SEQ ID NO 48
X	GenPept acc no AAB42225	SEQ ID NO 48
X	GenPept acc no AAC15584	SEQ ID NO 49
P(X)	GenPept acc no AAF69825	SEQ ID NO 50
X	GenPept acc no BAA18909	SEQ ID NO 51
X	GenPept acc no AAC 83205	SEQ ID NO 52

INTERNATIONAL SEARCH REPORT

International application No.

PCT/NZ00/00015

Box I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos :
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos :
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos :
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

The common feature of the polynucleotide and amino acid sequences of the present claims is that they are expressed in the stromal cells of the lymph glands of "flaky skin" mice, and not in 3T3 fibroblast cells. However, the specification discloses that at least some of the sequences are to known protein types. It is not considered that expression in one cell type rather than another is a special technical feature under Rule 13.2 of the PCT. This is particularly so as some of the protein types of the present application, eg fibroblast growth factor receptors, are known to be expressed in a variety of cell types.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

100

101

102

103

104

105

106

107

108

109

110

111

112

113

114

115

116

117

118

119

120

121

122

123

124

125

126

127

128

129

130

131

132

133

134

135

136

137

138

139

140

141

142

143

144

145

146

147

148

149

150

151

152

153

154

155

156

157

158

159

160

161

162

163

164

165

166

167

168

169

170

171

172

173

174

175

176

177

178

179

180

181

182

183

184

185

186

187

188

189

190

191

192

193

194

195

196

197

198

199

200